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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US00/08621 (22) International Filing Date: 31 March 2000 (31.03.00) (30) Priority Data: 60/127,607           31 March 1999 (31.03.99)   US 60/127,636           2 April 1999 (02.04.99)   US 60/127,728           5 April 1999 (05.04.99)   US 09/540,763           30 March 2000 (30.03.00)   US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications US                                   60/127,607 (CIP) Filed on                           31 March 1999 (31.03.99) US                                   60/127,636 (CIP) Filed on                           2 April 1999 (02.04.99) US                                   60/127,728 (CIP) Filed on                           5 April 1999 (05.04.99) US                                   09/540,763 (CIP) Filed on                           30 March 2000 (30.03.00) (71) Applicant (for all designated States except US): CURAGEN CORPORATION [US/US]; 555 Long Wharf Drive, 11th Floor, New Haven, CT 06511 (US).		(72) Inventors; and (75) Inventors/Applicants (for US only): SHIMKETS, Richard, A. [US/US]; 191 Leete Street, West Haven, CT 06516 (US). LEACH, Martin [GB/US]; 884 School Street, Webster, MA 01570 (US). (74) Agent: ELRIFI, Ivor, R.; Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, MA 02111 (US). (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published Without international search report and to be republished upon receipt of that report.	
(54) Title: NUCLEIC ACIDS INCLUDING OPEN READING FRAMES ENCODING POLYPEPTIDES; "ORFX"			
(57) Abstract			
<p>The present invention provides open reading frames ORFX, encoding isolated polypeptides, as well as polynucleotides encoding ORFX and antibodies that immunospecifically bind to ORFX or any derivative, variant, mutant, or fragment of the ORFX polypeptides, polynucleotides or antibodies. The invention additionally provides methods in which the ORFX polypeptide, polynucleotide and antibody are used in detection and treatment of a broad range of pathological states, as well as to other uses.</p>			

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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(22) International Filing Date: 14 January 1999 (14.01.99)		(74) Agents: GRANAHAH, Patricia et al.; Hamilton, Brook, Smith & Reynolds, P.C., Two Militia Drive, Lexington, MA 02421 (US).	
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60/071,374 15 January 1998 (15.01.98) US 60/093,491 20 July 1998 (20.07.98) US 60/110,941 4 December 1998 (04.12.98) US 09/232,197 14 January 1999 (14.01.99) US 09/232,200 14 January 1999 (14.01.99) US 09/232,201 14 January 1999 (14.01.99) US 09/232,195 14 January 1999 (14.01.99) US			
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(54) Title: FATTY ACID TRANSPORT PROTEINS			
(57) Abstract			
<p>A family of fatty acid transport proteins (FATPs) mediate transport of long chain fatty acids (LCFAs) across cell membranes into cells. These proteins exhibit different expression patterns among the organs of mammals. Nucleic acids encoding FATPs of this family, vectors comprising these nucleic acids, as well as the production of FATP proteins in host cells are described. Also described are methods to test FATPs for fatty acid transport function, and methods to identify inhibitors or enhancers of transport function. The altering of LCFA uptake by administering to the mammal an inhibitor or enhancer of FATP transport function of a FATP in the small intestine can decrease or increase calories available as fats, and can decrease or increase circulating fatty acids. The organ specificity of FATP distribution can be exploited in methods to direct drugs, diagnostic indicators and so forth to an organ such as the heart.</p>			

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## FATTY ACID TRANSPORT PROTEINS

## RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application Number 60/071,374 entitled "Identification of a Family of Fatty Acid Transporters Conserved From Mycobacterium to Man," by Andreas Stahl, David Hirsch and Harvey F. Lodish, filed on January 15, 1998; U.S. Provisional Application Number 60/093,491 entitled "Fatty Acid Transport Proteins," by Andreas Stahl, David J. Hirsch, Harvey F. Lodish, Ruth E. Gimeno and Louis A. Tartaglia, filed on July 20, 1998; and U.S. Provisional Application Number 60/110,941 entitled "Fatty Acid Transport Proteins," by Andreas Stahl, David J. Hirsch, Harvey F. Lodish, Ruth E. Gimeno and Louis A. Tartaglia, filed on December 4, 1998. This application also claims priority to Attorney's Docket Nos. WHI97-21p3MA, WHI97-21p3MB, WHI97-21p3MC, WHI97-21p3MD, each of which is entitled "Fatty Acid Transport Proteins," by Andreas Stahl, David J. Hirsch, Harvey F. Lodish, Ruth E. Gimeno and Louis A. Tartaglia, filed on January 14, 1999. The teachings of each of these referenced applications are incorporated herein by reference in their entirety.

## GOVERNMENT SUPPORT

The invention was supported, in whole or in part, by National Institutes of Health Grant DK 47618 and National Institutes of Health Grant 5 T32 CA 09541. The United States Government has certain rights in the invention.



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## BACKGROUND OF THE INVENTION

Long chain fatty acids (LCFAs) are an important source of energy for most organisms. They also function as blood hormones, regulating key metabolic functions such as hepatic glucose production. Although LCFAs can diffuse through the hydrophobic core of the plasma membrane into cells, this nonspecific transport cannot account for the high affinity and specific transport of LCFAs exhibited by cells such as cardiac muscle, hepatocytes, enterocytes, and adipocytes. The molecular mechanisms of LCFA transport remains largely unknown. Identifying these mechanisms can lead to pharmaceuticals that modulate fatty acid uptake by the intestine and by other organs, thereby alleviating certain medical conditions (e.g. obesity).

## SUMMARY OF THE INVENTION

Described herein is a diverse family of fatty acid transport proteins (FATPs) which are evolutionarily conserved; these FATPs are plasma membrane proteins which mediate transport of LCFAs across the membranes and into cells. Members of the FATP family described herein are present in a wide variety of organisms, from mycobacteria to humans, and exhibit very different expression patterns in tissues among the organisms. FATP family members are expressed in prokaryotic and eukaryotic organisms and comprise characteristic amino acid domains or sequences which are highly conserved across family members. In addition, the function of the FATP gene family is conserved throughout evolution, as shown by the fact that the *Caenorhabditis* (*C. elegans*) and mycobacterial FATPs described herein facilitate LCFA uptake when they are overexpressed in COS cells or *Escherichia* (*E. coli*), respectively. FATPs are expressed in a wide variety of tissues, including all tissues which are important to fatty acid metabolism (uptake and processing).

In specific embodiments, FATPs of the present invention are from such diverse organisms as humans (*Homo* (*H.*) *sapiens*), mice, (*Mus* (*M.*) *musculus*), *F. rubripes*, *C. elegans*, *Drosophila* (*D.*) *melanogaster*, *Saccharomyces* (*S.*) *cerevisiae*, *Aspergillus*

*nidulans*, *Cochliobolus heterostrophus*, *Magnaporthe grisea* and *Mycobacterium (M.)*, such as *M. tuberculosis*. As described herein, four novel mouse FATPs, referred to as mmFATP2, mmFATP3, mmFATP4 and mmFATP5, and six human FATPs, referred to as hsFATP1, hsFATP2, hsFATP3, hsFATP4, hsFATP5 and hsFATP6, have been  
5 identified. All four novel murine FATPs (mmFATP2-5) and a previously identified murine FATP (renamed herein FATP1) have orthologs in humans (hsFATP1-5); the sixth human FATP (hsFATP6) does not as yet have a mouse ortholog. The expression patterns of these FATPs vary, as described in detail below.

The present invention relates to FATP family members from prokaryotes and  
10 eukaryotes, nucleic acids (DNA, RNA) encoding FATPs, and nucleic acids which are useful as probes or primers (e.g., for use in hybridization methods, amplification methods) for example, in methods of detecting FATP-encoding genes, producing FATPs, and purifying or isolating FATP-encoding DNA or RNA. Also the subject of this invention are antibodies (polyclonal or monoclonal) which bind an FATP or  
15 FATPs; methods of identifying additional FATP family members (for example, orthologs of those FATPs described herein by amino acid sequence) and variant alleles of known FATP genes; methods of identifying compounds which bind to an FATP, or modulate or alter (enhance or inhibit) FATP function; compounds which modulate or alter FATP function; methods of modulating or altering (enhancing or inhibiting) FATP  
20 function and, thus, LCFA uptake into tissues of a mammal (e.g. human) by administering a compound or molecule (a drug or agent) which increases or reduces FATP activity; and methods of targeting compounds to tissues by administering a complex of the compound to be targeted to tissues and a component which is bound by an FATP present on cells of the tissues to which the compound is to be targeted. For  
25 example, a complex of a drug to be delivered to the liver and a component which is bound by an FATP present on liver cells (e.g., FATP5) can be administered.

In one embodiment, the present invention relates to modulating or altering (enhancing or inhibiting/reducing) LCFA uptake in the small intestine and, thus,

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increasing or reducing the number of calories in the form of fats available to an individual. In another embodiment, the present invention relates to inhibiting or reducing LCFA uptake in the small intestine in order to reduce circulating fatty acid levels; that is, LCFA uptake in the small intestine is reduced and, therefore, circulating (blood) levels are not as high as they otherwise would be. FATP4 has been shown to be expressed in epithelial cells of the small intestine and particularly in the brush border layer of the small intestine. FATP2 has also been shown to be expressed at low levels in epithelial cells of the small intestine, particularly in the duodenum. In contrast, FATP1, FATP3, FATP5 and FATP6 were not detected in any of the intestinal tissues.

Thus, also described herein are FATPs which are present in the epithelial cell layer of the small intestine where they mediate LCFA uptake. These FATPs, particularly FATP4 and also FATP2, are targets for methods and drugs which block their function or activity and are useful in treating obesity, diabetes and heart disease. The ability of these FATPs to mediate fat uptake can be modulated or altered (enhanced or inhibited), thus modulating fat uptake in the small intestine. This can be done, for example, by administering to an individual, such as a human or other animal, a drug which blocks interaction of LCFAs with FATP4 and/or FATP2 in the small intestine, thus inhibiting LCFA passage into the cells of the small intestine. As a result, fat absorption is reduced and, although the individual has consumed a certain quantity of fat, the LCFAs are not absorbed to the same extent they would have been in the absence of the compound administered.

Thus, one embodiment of this invention is a method of reducing LCFA uptake (absorption) in the small intestine and, as a result, reducing caloric uptake in the form of fat. A further embodiment is a compound (drug) useful in inhibiting or reducing fat absorption in the small intestine. In another embodiment, the invention is a method of reducing circulating fatty acid levels by administering to an individual a compound which blocks interactions of LCFAs with FATP4 and/or FATP2 in the small intestine, thus inhibiting LCFA passage into cells of the small intestine. As a result, fatty acids

pass into the circulatory system at a diminished level and/or rate, and circulating fatty acid levels are lower than they would be in the absence of the compound administered. This method is particularly useful for therapy in individuals who are at risk for or have hyperlipidemia. That is, it can be used to prevent the occurrence of elevated levels of  
5 lipids in the blood or to treat an individual in whom blood lipid levels are elevated. Also the subject of this invention is a method of identifying compounds which alter FATP function (and thus, in the case of FATP2 and/or FATP4, alter LCFA uptake in the small intestine).

In another embodiment, the present invention relates to a method of modulating  
10 or altering (enhancing or inhibiting) the function of FATP6, which is expressed at high levels in the heart. A method of inhibiting FATP6 function is useful, for example, in individuals with heart disease, such as ischemia, since reducing LCFA uptake into heart muscle in an individual who has ischemic heart disease, which may be manifested by, for example, angina or heart attack, can reduce symptoms or reduce the extent of  
15 damage caused by the ischemia. In this embodiment, a drug which inhibits FATP6 function is administered to an individual who has had or is having a heart attack, to reduce LCFA uptake by the individual's heart and, as a result, reduce the damage caused by ischemia. In a further embodiment, this invention is a method of targeting a compound, such as a therapeutic drug or an imaging reagent, to heart tissue by  
20 administering to an individual (e.g., a human) a complex of the compound and a component (e.g., a LCFA or LCFA-like compound) which is bound by an FATP (e.g., FATP6) present in cells of heart tissue.

In a further embodiment, LCFA uptake by the liver is modulated or altered (enhanced or reduced), in an individual. For example, a drug which inhibits the  
25 function of an FATP present in liver (e.g., FATP5) is administered to an individual who is diabetic, in order to reduce LCFA uptake by liver cells and, thus reduce insulin resistance.

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The present invention, thus, provides methods which are useful to alter, particularly reduce, LCFA uptake in individuals and, as a result, to alter (particularly reduce), availability of the LCFAs for further metabolism. In a specific embodiment, the present invention provides methods useful to reduce LCFA uptake and, thus, fatty acid metabolism in individuals, with the result that caloric availability from fats is reduced, and circulating fatty acid levels are lower than they otherwise would be. These methods are useful, for example, as a means of weight control in individuals, (e.g., humans) and as a means of preventing elevated serum lipid levels or reducing serum lipid levels in humans. FATPs expressed in the small intestine, such as FATP4, are useful targets to be blocked in treating obesity (e.g., chronic obesity) or to be enhanced in treating conditions in which enhanced LCFA uptake is desired (e.g., malabsorption syndrome or other wasting conditions).

The identification of this evolutionarily conserved fatty acid transporter family will allow a better understanding of the mechanisms whereby LCFAs traverse the lipid bilayer as well as yield insight into the control of energy homeostasis and its dysregulation in diseases such as diabetes and obesity.

#### BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the amino acid sequence alignment of FATPs: mmFATP1 (SEQ ID NO:92), mmFATP2 (SEQ ID NO:93), mmFATP3 (SEQ ID NO:94), mmFATP4 (SEQ ID NO:95), mmFATP5 (SEQ ID NO:96), ceFATPa (SEQ ID NO:97), scFATP (SEQ ID NO:98) and mtFATP (SEQ ID NO:99). The underlining (amino acid residues 204-212 of mtFATP) indicates an AMP binding motif which is found in many classes of proteins; the underlining at amino acid residues 204-507 of the mtFATP sequence indicates the FATP 360 amino acid signature sequence.

Figures 2A-2D show results of LCFA uptake assays. Figures 2A-2D: COS cells were cotransfected using the DEAE-dextran method with the mammalian expression vectors pCDNA-CD2 either alone (control; Figure 2A) or in combination

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with one of the FATP-containing expression vectors (pCDNA-mmFATP1, Figure 2B; pCDNA-mmFATP2, Figure 2C; or pCMV-SPORT2-mmFATP5, Figure 2D) as described in Materials and Methods for Example 2. COS cells were gated on forward scatter (FSC) and side scatter (SS), and the results shown represent >10,000 cells. Cells  
5 exhibiting >300 CD2 fluorescence units (vertical line) representing 15% of all cells were deemed CD2 positive.

Figure 3 is a graph of fluorescence of cells expressing a FATP gene. As in Figures 2A-2D, COS cells were cotransfected with pCDNA-CD2 either alone (control) or in combination with one of the FATP-containing expression vectors (pCDNA-mmFATP1, pCDNA-mmFATP2, pCMV-SPORT2-mmFATP5, or pCDNA-ceFATPb).  
10 The mean BODIPY-FA fluorescence of the CD2-positive cells is plotted; results shown represent the average of three experiments, each consisting of greater than 50,000 COS cells. Note that a logarithmic scale is used on the ordinate.

Figure 4 is a graph of the uptake of palmitate with time. The full-length coding  
15 region of mtFATP (squares) or a control protein (TFE3; circles) was subcloned into the inducible, prokaryotic expression vector pET (Novagen). Expression from the resulting plasmid was induced (solid symbols) in transformed *E. coli* cells with 1 mM isopropyl- $\beta$ -D-thiogalactoside (IPTG) for 1 hour, or cells were left uninduced (open symbols). Data points were done in triplicate and counts were normalized to the number of  
20 bacteria as determined by OD<sub>600</sub>.

Figure 5 is a phylogenetic tree produced by aligning complete and partial sequences for *FATP* genes from human, rat, mouse, puffer fish, *D. melanogaster*, *C. elegans*, *S. cerevisiae*, and *M. tuberculosis* using ClustalX and using these data to produce a phylogenetic tree using TreeViewPPC. The bar indicates the number of  
25 substitutions per residue, i.e., 0.1 corresponds to a distance of 10 substitutions per 100 residues.

Figure 6 shows a comparison of the FATP signature sequences of mmFATP1 (SEQ ID NO:1), mmFATP5, (SEQ ID NO:2), ceFATPa (SEQ ID NO:3), scFATP (SEQ ID NO:4) and mtFATP (SEQ ID NO:5).

Figure 7 shows the sequence identity among the FATP family members and  
5 VLACs, based on the 360 amino acid signature sequence of FATP from Figure 1.  
Figures 8A and 8B are the mmFATP3 DNA sequence (SEQ ID NO:6).  
Figure 9 is the mmFATP3 protein sequence (SEQ ID NO:7).  
Figures 10A and 10B are the mmFATP4 DNA sequence (SEQ ID NO:8).  
Figure 11 is the mmFATP4 protein sequence (SEQ ID NO:9).  
10 Figures 12A and 12B are the mmFATP5 DNA sequence (SEQ ID NO:10).  
Figure 13 is the mmFATP5 protein sequence (SEQ ID NO:11).  
Figures 14A and 14B are the hsFATP2 DNA sequence (SEQ ID NO:12).  
Figure 15 is the hsFATP2 protein sequence (SEQ ID NO:13).  
Figures 16A and 16B are the hsFATP3 DNA sequence (SEQ ID NO:14).  
15 Figure 17 is the hsFATP3 protein sequence (SEQ ID NO:15).  
Figures 18A and 18B are the hsFATP4 DNA sequence (SEQ ID NO:16).  
Figure 19 is the hsFATP4 protein sequence (SEQ ID NO:17).  
Figures 20A and 20B are the hsFATP5 DNA sequence (SEQ ID NO:18).  
Figure 21 is the hsFATP5 protein sequence (SEQ ID NO:19).  
20 Figures 22A and 22B are the hsFATP6 DNA sequence (SEQ ID NO:20).  
Figure 23 is the hsFATP6 protein sequence (SEQ ID NO:21).  
Figures 24A and 24B are the mtFATP DNA sequence (SEQ ID NO:22).  
Figure 25 is the mtFATP protein sequence (SEQ ID NO:23).  
Figure 26 shows the DNA sequence (SEQ ID NO:24) and predicted amino acid  
25 sequence (SEQ ID NO:25) of human FATP1.  
Figure 27 shows the DNA sequence (SEQ ID NO:26) and predicted amino acid  
sequence (SEQ ID NO:27) of human FATP4.

Figure 28A is a hydrophobicity plot for hsFATP1, showing that it has multiple membrane-spanning domains.

Figure 28B is the amino acid composition of hsFATP1.

Figure 28C is a hydrophilicity plot for hsFATP1, made using the Kyte-Doolittle  
5 method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figure 29A is a hydrophobicity plot for hsFATP4, showing that it has multiple membrane-spanning domains.

Figure 29B is a listing of the amino acid composition of hsFATP4.

Figure 29C is a hydrophilicity plot for hsFATP4, made using the Kyte-Doolittle  
10 method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figures 30A and 30B show a comparison of the nucleotide sequence of human FATP1 (SEQ ID NO:28) and the nucleotide sequence of mouse FATP1 (SEQ ID NO:29).

Figures 31A and 31B show a comparison of the nucleotide sequence of human  
15 FATP4 (SEQ ID NO:30) and the nucleotide sequence of mouse FATP4 (SEQ ID NO:31).

Figure 32 shows a comparison of the amino acid sequence of human FATP1 (SEQ ID NO:32) and the amino acid sequence of mouse FATP1 (SEQ ID NO:33). Shaded amino acid residues match the consensus sequence exactly

20 Figure 33 shows a comparison at the amino acid level of human FATP4 (SEQ ID NO:34) and mouse FATP4 (SEQ ID NO:35). Shaded amino acid residues match the consensus sequence exactly.

Figure 34 shows the nucleotide sequence (SEQ ID NO:36) and predicted amino acid sequence (SEQ ID NO:37) of hsFATP6.

25 Figure 35A is a hydrophobicity plot for hsFATP6, showing that it has multiple membrane-spanning domains.

Figure 35B is a listing of the amino acid composition of hsFATP6.



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Figure 35C is a hydrophilicity plot for hsFATP6, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figure 36 shows an alignment of the amino acid sequences of hsFATP1 (SEQ ID NO:38), hsFATP4 (SEQ ID NO:39) and hsFATP6 (SEQ ID NO:40). Shaded amino acid residues match the consensus sequence exactly.

Figure 37 shows results of assessment of fatty acid uptake by human FATP1 and human FATP4. The percent of CD2-positive cells exhibiting a BODIPY-fluorescence of more than 300 arbitrary units is plotted for the three different conditions tested.

Figure 38 is a graph showing uptake of tritiated oleate, with time, by 293 cells transfected with either (diamonds) a plasmid for expression of human FATP4 or (squares) a control plasmid.

Figure 39 is an illustration of the amino acid sequences of human FATP4 (SEQ ID NO:41) and mouse FATP4 (SEQ ID NO:42) compared to human FATP1 (SEQ ID NO:43). Shown by underlining are the FATP consensus sequence (236-556 of hsFATP1) and the AMP-binding motif (246-254 of hsFATP1). The human FATPs were cloned by screening libraries with sequences from ESTs (expressed sequence tags). Mouse FATP4 was cloned by PCR using degenerate primers.

Figure 40 is a graph showing the uptake, with time, of tritiated oleate by mouse enterocytes in the presence of no oligonucleotide (squares), sense oligonucleotide (circles) or antisense oligonucleotide (diamonds).

Figure 41 is a bar graph showing uptake of tritiated oleate, by mouse enterocytes in the presence of various concentrations of antisense (solid bars), mismatch (stippled bars) or sense (lined bars) oligonucleotides.

Figure 42 is a bar graph showing uptake of tritiated oleate and uptake of <sup>35</sup>S-labeled methionine by mouse enterocytes to which were added no oligonucleotide, the antisense oligonucleotide, or the mismatch oligonucleotide.

Figure 43A is the nucleotide sequence of the gene encoding mouse FATP4 (SEQ ID NO:44).

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Figure 43B is the amino acid sequence of mouse FATP4 protein (SEQ ID NO:45).

Figures 44A, 44B, and 44C are the hsFATP1 DNA sequence (SEQ ID NO:46).  
Coding region: 175-2115 (1941 nt).

5 Figure 45 is the hsFATP1 protein sequence (SEQ ID NO:47).

Figures 46A and 46B are the hsFATP2 DNA sequence (SEQ ID NO:48).  
Coding region: 223-2085 (1863 nt).

Figure 47 is the hsFATP2 protein sequence (SEQ ID NO:49).

Figure 48 is the partial DNA sequence of hsFATP3 (SEQ ID NO:50). Coding  
10 region: 1-993.

Figure 49 is the partial protein sequence of hsFATP3 (SEQ ID NO:51).

Figures 50A, 50B, and 50C are the hsFATP4 DNA sequence (SEQ ID NO:52).  
Coding region: 208-2139 (1932 nt).

Figure 51 is the hsFATP4 protein sequence (SEQ ID NO:53).

15 Figure 52 is the hsFATP5 partial DNA sequence (SEQ ID NO:54). Coding  
region: 1-1062.

Figure 53 is the hsFATP5 partial protein sequence (SEQ ID NO:55).

Figures 54A, 54B, and 54C are the hsFATP6 DNA sequence (SEQ ID NO:56).  
Coding region: 643-2502 (1860 nt).

20 Figure 55 is the hsFATP6 protein sequence (SEQ ID NO:57).

Figures 56A, 56B, and 56C are the mFATP1 DNA sequence (m=*Rattus  
norvegicus*; (SEQ ID NO:58). Coding region: 75-2015 (1941 nt).

Figure 57 is the mFATP1 protein sequence (SEQ ID NO:59).

Figure 58A, 58B, and 58C are the mFATP2 DNA sequence (SEQ ID NO:60).  
25 Coding region: 795-2657 (1863 nt).

Figure 59 is the mFATP2 protein sequence (SEQ ID NO:61).

Figure 60A and 60B are the mFATP4 partial DNA sequence (SEQ ID NO:62).  
Coding region: 1-1218.

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Figure 61 is the mFATP4 partial DNA sequence (SEQ ID NO:63).

Figure 62A, 62B, and 62C are the mmFATP1 DNA sequence (SEQ ID NO:64).

Coding region: 1-1944.

Figure 63 is the mmFATP1 protein sequence (SEQ ID NO:65).

5        Figures 64A and 64B are the mmFATP2 DNA sequence (SEQ ID NO:66).

Coding region: 121-1992 (1872 nt).

Figure 65 is the mmFATP2 protein sequence (SEQ ID NO:67).

Figures 66A and 66B are the mmFATP3 partial DNA sequence (SEQ ID NO:68). Coding region: 1-1830.

10        Figure 67 is the mmFATP3 partial protein sequence (SEQ ID NO:69).

Figures 68A, 68B, and 68C are the mmFATP4 DNA sequence (SEQ ID NO:70).

Coding region: 1-1932.

Figures 69 is the mmFATP4 protein sequence (SEQ ID NO:71).

Figures 70A and 70B are the mmFATP5 DNA sequence (SEQ ID NO:72).

15        Coding region: 60-2129.

Figure 71 is the mmFATP5 protein sequence (SEQ ID NO:73).

Figures 72A and 72B are the dmFATP partial DNA sequence (dm=*Drosophila melanogaster*; SEQ ID NO:74). Coding region: 1-1773.

Figures 73 is the dmFATP partial protein sequence (SEQ ID NO:75).

20        Figure 74 is the drFATP partial DNA sequence (dr=*Danio rerio*, zebrafish; SEQ ID NO:76) Coding region: 1-173.

Figure 75 is the drFATP partial protein sequence (SEQ ID NO:77).

Figure 76A and 76B are the ceFATPa DNA sequence (SEQ ID NO:78). Coding region: 1-1953.

25        Figure 77 is the ceFATPa protein sequence (SEQ ID NO:79).

Figures 78A and 78B are the ceFATPb DNA sequence (SEQ ID NO:80).

Coding region: 1-1968.

Figure 79 is the ceFATPb protein sequence (SEQ ID NO:81).

Figures 80A and 80B are the chFATP DNA sequence (SEQ ID NO:82; ch=*Cochliobolu heterostrophus*). Coding region: 1-1932.

Figure 81 is the chFATP protein sequence (SEQ ID NO:83).

Figure 82 is the anFATP partial protein sequence (an=*Aspergillus nidulans*;  
5 SEQ ID NO:84). Coding region: 1-597.

Figure 83 is the anFATP partial protein sequence (SEQ ID NO:85).

Figure 84 is the mgFATP partial DNA sequence (mg=*Magnaporthe grisea*, rice blast; SEQ ID NO:86). Coding region: 1-522.

Figure 85 is the mgFATP partial protein sequence (SEQ ID NO:87).

10 Figures 86A and 86B are the scFATP DNA sequence (SEQ ID NO:88). Coding region: 1-1872.

Figure 87 is the scFATP protein sequence (SEQ ID NO:89).

Figures 88A and 88B are the mtFATP DNA sequence (SEQ ID NO:90).

Figure 89 is the mtFATP protein sequence (SEQ ID NO:91). Coding region: 1-  
15 1794.

Figure 90 is a concensus sequence of the FATP signature sequence (SEQ ID NO:

100), based on 23 independent sequences aligned in ClustalX. The height of the bar at each amino acid residue position indicates the degree of conservation at that position.

20 Gaps have been inserted to maintain the strength of the alignment.

Figure 91 is a hydrophilicity plot for hsFATP2, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

Figure 92 is a hydrophilicity plot for the hsFATP3 partial protein, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues  
25 at a time.

Figure 93 is a hydrophilicity plot for the hsFATP5 partial protein, made using the Kyte-Doolittle method, averaging hydrophilicity values for 18 amino acid residues at a time.

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Figures 94A and 94B are a representation of the DNA sequence (SEQ ID NO:101) of the hsFATP5 gene, and the amino acid sequence (SEQ ID NO:102) of the hsFATP5 protein.

#### DETAILED DESCRIPTION OF THE INVENTION

5 As described herein, FATPs are a large evolutionarily conserved family of proteins that mediate the transport of LCFAs into cells. The family includes proteins which are conserved from mycobacteria to humans and exhibit very different expression patterns in tissues. Specific embodiments described include FATPs from mice, humans, nematodes, fungi and mycobacteria which have been shown to be functional LCFA  
10 transporters. The term "fatty acid transport proteins" ("FATPs") as used herein, refers to the proteins described herein as FATP1, FATP2, FATP3, FATP4, FATP5 and FATP6, which have been described in one or more species of mammals, as well as mtFATP, ceFATP, scFATP, anFATP, mgFATP, and chFATP, and other proteins sharing at least about 50% amino acid sequence similarity, preferably at least about 60%  
15 sequence similarity, more preferably at least about 70% sequence similarity, and still more preferably, at least about 80% sequence similarity, and most preferably, at least about 90% sequence similarity in the approximately 360 amino acid signature sequence. The approximately 360 amino acid FATP signature sequence is shown in Figure 1. The consensus sequence of the signature sequence is shown in Figure 90. The nomenclature  
20 used herein to refer to FATPs includes a species-specific prefix (e.g., mm, *Mus musculus*; hs or h, *Homo sapiens* or human; mt *M. tuberculosis*; dm, *D. melanogaster*; ce, *C. elegans*; sc, *Saccharomyces cerevisiae*) and a number such that mammalian homologues in different species share the same number. For example, six human and five mouse *FATP* genes which are expressed in a variety of tissues are described herein  
25 and are referred to, respectively, as hsFATP1-hsFATP6 and mmFATP1-mmFATP5; for example, hsFATP4 and mmFATP4 are the human and mouse orthologs.

Expression patterns of human and mouse FATPs have been assessed and are described below. Briefly, results of these assessments show that FATP5 is a liver-specific gene. FATP2 is highly expressed in liver and kidney. Both of these proteins, as well as FATP4 and FATPs from nematodes and mycobacteria, have been shown to be functional LCFA transporters. Results have also shown that FATP4 mRNA is present at high levels in epithelial cells of two regions of the small intestine (the jejunum and ileum) and at lower, but significant, levels in a third region (the duodenum). They further showed that FATP2 mRNA is present in epithelial cells of the duodenum at a level similar to that of FATP4 mRNA levels, but is present at lower levels in the jejunum and ileum. FATP4 mRNA was absent from other cell types of the small intestine and no FATP4 mRNA could be detected in any cells of the colon. No signals above background could be detected for FATP1, FATP3 and FATP5 in any of the intestinal tissues. Thus, FATP4 is the major FATP in the mouse small intestine, which supports a major role for FATP4 (along with FATP2 to a lesser extent) in absorption of free fatty acids. hsFATP4 was clearly expressed in the jejunum and ileum; expression was absent in the stomach. This, too, is consistent with a major role for FATP4 in absorption of fatty acids in the human gut. Analysis of FATP expression in human tissues, also described in detail below, showed that hsFATP6, which has no mouse ortholog as yet, is expressed at high levels in the heart and at low levels in the placenta, but is undetectable in the other tissues assessed (Example 9). This is consistent with a major role for FATP6 in absorption of fatty acids in the heart.

Long chain fatty acids (LCFAs) are an important energy source for pro- and eukaryotes and are involved in diverse cellular processes, such as membrane synthesis, intracellular signaling, protein modification, and transcriptional regulation. In developed Western countries, human dietary lipids are mainly di- and triglycerides and account for approximately 40% of caloric intake (Weisburger, J. H. (1997) *J. Am. Diet. Assoc.* 97:S16-S23). These lipids are broken down into fatty acids and glycerol by pancreatic lipases in the small intestine (Chapus, C., Rovey, M., Sarda, L. & Verger, R.

(1988) *Biochimie* 70:1223-34); LCFAs are then transported into brush border cells, where the majority is re-esterified and secreted into the lymphatic system as chylomicrons (Green, P.H. & Riley, J.W. (1981) *Aust. N.Z.J. Med.* 11:84-90). Fatty acids are liberated from lipoproteins by the enzyme lipoprotein lipase, which is bound to the luminal side of endothelial cells (Scow, R.O. & Blachette-Mackie, E.J. (1992) *Mol. Cell. Biochem* 116:181-191). "Free" fatty acids in the circulation are bound to serum albumin (Spector, A.A. (1984) *Clin. Physiol. Biochem* 2:123-134) and are rapidly incorporated by adipocytes, hepatocytes, and cardiac muscle cells. The latter derive 60-90% of their energy through the oxidation of LCFAs (Neely, J.F. Rovetto, M.J. & Oram, J.F. (1972) *Prog. Cardiovasc. Dis.* 15:289-329). Although saturable and specific uptake of LCFAs has been demonstrated for intestinal cells, hepatocytes, cardiac myocytes, and adipocytes, the molecular mechanisms of LCFA transport across the plasma membrane have remained controversial (Hui, T.Y. & Bernlohr, D.A. (1997) *Front. Biosci.* 15:d222-31-d231; Schaffer, J.E. & Lodish, H.F. (1995) *Trends Cardiovasc. Med.* 5:218-224). Described herein is a large family of highly homologous mammalian LCFA transporters which show wide expression, including in all tissues relevant to fatty acid metabolism. Further described are novel members of this family in other species, including mycobacterial and nematode FATPs which, like their mammalian counterparts, are functional fatty acid transporters.

20       The discovery of a diverse but highly homologous family of FATPs is reminiscent of the glucose transporter family. In a manner similar to the FATPs, the glucose transporters have very divergent patterns of tissue expression (McGowan, K.M., Long, S.D. & Pekala, P.H. (1995) *Pharmacol. Ther.* 66:465-505). The FATPs, like glucose transporters, may also differ in their substrate specificities, uptake kinetics, and hormonal regulation (Thorens, B. (1996) *Am. J. Physiol.* 270:G541-G553). Indeed, the levels of fatty acids in the blood, like those of glucose, can be regulated by insulin and are dysregulated in diseases such as noninsulin-dependent diabetes and obesity (Boden, G. (1997) *Diabetes* 46:3-10). The underlying mechanisms for the regulation of free

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fatty acid concentrations in the blood are not understood, but could be explained by hormonal modulation of FATPs.

Insulin-resistance is thought to be the major defect in non insulin-dependent diabetes mellitus (NIDDM) and is one of the earliest manifestations of NIDDM (McGarry (1992) *Science* 258:766-770). Free fatty acids (FFAs) may provide an explanation for why obesity is a risk factor for NIDDM. Plasma levels of FFAs are elevated in diabetic patients (Reaven *et al.* (1988) *Diabetes* 37:1020). Elevated plasma free fatty acids (FFAs) have been demonstrated to induce insulin-resistance in whole animals and humans (Boden (1998) *Front. Biosci.* 3:D169-D175). This insulin-resistance is likely mediated by effects of FFAs on a variety of issues. FFAs added to adipocytes *in vitro* induce insulin resistance in this cell type as evidenced by inhibition of insulin-induced glucose transport (Van Epps-Fung *et al.* (1997) *Endocrinology* 138:4338-4345). Rats fed a high fat diet developed skeletal muscle insulin resistance as evidenced by a decrease in insulin-induced glucose uptake by skeletal muscle (Han *et al.*, (1997) *Diabetes* 46:1761-1767). In addition, elevated plasma FFAs increase insulin-suppressed endogenous glucose production in the liver (Boden (1998) *Front. Biosci.* 3:D169-D175), thus increasing hepatic glucose output. It has been postulated that the adverse effects of plasma free fatty acids are due to the FFAs being taken up into the cell, leading to an increase in intracellular long chain fatty acyl CoA; intracellular long chain acyl CoAs are thought to mediate the effects of FFAs inside the cell. Thus, fatty acid induced insulin-resistance may be prevented by blocking uptake of FFAs into select tissues, in particular liver (by blocking FATP2 and/or FATP5), adipocyte (by blocking FATP1), and skeletal muscle (by blocking FATP1). Blocking intestinal fat absorption (by blocking FATP4) is also expected to reduce plasma FFA levels and thus improve insulin resistance.

During the pathogenesis of NIDDM insulin-resistance can initially be counteracted by increasing insulin output by the pancreatic beta cell. Ultimately, this compensation fails, beta cell function decreases and overt diabetes results (McGarry



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(1992) *Science* 258: 766-770). Manipulating beta cell function is a second point where fatty acid transporter blockers may be beneficial for diabetes. While no FATP homolog has been identified so far that is expressed in the beta cell of the pancreas, the data described below suggest the existence of such a transporter and the sequence

5 information included herein provides the means to identify such a transporter by degenerate PCR, using primers to regions conserved in all FATP family members or by low stringency hybridization. It has been demonstrated that exposure of pancreatic beta-cells to FFAs increases the basal rate of insulin secretion; this in turn leads to a decrease in the intracellular stores of insulin, resulting in decreased capacity for insulin

10 secretion after chronic exposure (Bollheimer *et al.*, (1998) *J. Clin. Invest.* 101:1094-1101). The effects of FFAs are again likely to be mediated by intracellular long chain fatty acyl CoA molecules (Liu *et al.*, (1998) *J. Clin. Invest.* 101:1870-1875). FFAs have also been demonstrated to increase beta cell apoptosis (Shimabukuro *et al.*, (1998) *Proc. Nat. Acad. Sci. USA* 95:2498-2502), possibly contributing to the decrease in beta

15 cell numbers in late stage NIDDM.

Another finding with potentially broad implications is the identification of a FATP homologue in *M. tuberculosis*. Tuberculosis causes more deaths worldwide than any other infectious agent and drug-resistant tuberculosis is re-emerging as a problem in industrialized nations (Bloom, B.R. & Small, P.M. (1998) *N. Engl. J. Med.* 338:677-

20 678). *Mycobacterium tuberculosis* has about 250 enzymes involved in fatty acid metabolism, compared with only about 50 in *E. coli*. It has been suggested that, living as a pathogen, the mycobacteria are largely lipolytic, rather than lipogenic, relying on the lipids within mammalian cells and the tubercle (Cole, S.T. *et al.*, *Nature* 393:537-544 (1998)). The *de novo* synthesis of fatty acids in *Mycobacterium leprae* is

25 insufficient to maintain growth (Wheeler, P.R., Bulmer, K & Ratledge, C. (1990) *J. Gene. Microbiol.* 136:211-217). Thus, it is reasonable to expect that inhibitors of mtFATP will serve as therapeutics for tuberculosis. FATPs expressed in mycobacteria can be targeted to reduce or prevent replication of mycobacteria (e.g., to reduce or

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prevent replication of *M. tuberculosis*) and, thus, reduce or prevent their adverse effects. For example, a FATP or FATPs expressed by *M. tuberculosis* can be targeted and inhibited, thus reducing or preventing growth of this pathogen (and tuberculosis in humans and other mammals). An inhibitor of an *M. tuberculosis* FATP can be  
5 identified, using methods described herein (e.g., expressing the FATP in an appropriate host cell, such as *E. coli* or COS cells; contacting the cells with an agent or drug to be assessed for its ability to inhibit the FATP and, as a result, mycobacterial growth, and assessing its effects on growth). A drug or agent identified in this manner can be further tested for its ability to inhibit a *M. tuberculosis* FATP and *M. tuberculosis* infection in  
10 an appropriate animal model or in humans. A method of inhibiting mycobacterial growth, particularly growth of *M. tuberculosis*, and compounds useful as drugs for doing so are also the subject of this invention.

An isolated polynucleotide encoding mtFATP, like other polynucleotides encoding FATPs of the FATP family, can be incorporated into vectors, nucleic acids of  
15 viruses, and other nucleic acid constructs that can be used in various types of host cells to produce mtFATP. This mtFATP can be used, as it appears on the surface of cells, or in various artificial membrane systems, to assess fatty acid transport function, to identify ligands and molecules that are modulators of fatty acid transport activity. Molecules found to be inhibitors of mtFATP function can be incorporated into  
20 pharmaceutical compositions to administer to a human for the treatment of tuberculosis.

Particular embodiments of the invention are polynucleotides encoding a FATP of *Cochliobolus (Helminthosporium) heterostrophus* or portions or variants thereof, the isolated or recombinantly produced FATP, methods for assessing whether an agent binds to the chFATP, and further methods for assessing the effect of an agent being  
25 tested for its ability to modulate fatty acid transport activity. *Cochliobolus heterostrophus* is an ascomycete that is the cause of southern corn leaf blight, an economically important threat to the corn crop in the United States. The related species *C. sativus* causes crown rot and common root rot in wheat and barley. One or more

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FATPs of *C. heterostrophus* can be targeted for the identification of an inhibitor of chFATP function, which can be then be used as an agent effective against infection of plants by *C. heterostrophus* and related organisms. Methods described herein that were applied in studying the expression of a FATP gene and the function of the FATP in its natural site of expression or in a host cell, can be used in the study of the chFATP gene and protein.

*Magnaporthe grisea* (rice blast) is an economically important fungal pathogen of rice. Further embodiments of the invention are nucleic acid molecules encoding a FATP of *Magnaporthe grisea*, portions thereof, or variants thereof, isolated mgFATP, nucleic acid constructs, and engineered cells expressing mgFATP. Other aspects of the invention are assays to identify an agent which binds to mgFATP and assays to identify an agent which modulates the function of mgFATP in cells in which mgFATP is expressed or in artificial membrane systems. Agents identified as inhibiting mgFATP activity can be developed into anti-fungal agents to be used to treat rice infected with rice blast.

*Caenorhabditis elegans* is a nematode related to plant pathogens and human parasites. An isolated polynucleotide which encodes ceFATP, like other polynucleotides encoding FATPs of the FATP family described herein, can be incorporated into nucleic acid vectors and other constructs that can be used in various types of cells to produce ceFATP. ceFATP as it occurs in cells or as it can be isolated or incorporated into various artificial or reconstructed membrane systems, can be used to assess fatty acid transport, and to identify ligands and agents that modulate fatty acid transport activity. Agents found by such assays to be inhibitors of ceFATP activity can be incorporated into compositions for the treatment of diseases caused by genetically related organisms with a FATP of similar sensitivity to the agents.

*Aspergillus nidulans* is one of a family of fungal species that can infect humans. Further embodiments of the invention of the family of polynucleotides encoding FATPs are polynucleotides encoding a FATP of *Aspergillus nidulans*, and vectors and host

cells that can be constructed to comprise such polynucleotides. Further embodiments are a polypeptide encoded by such polynucleotides, portions thereof having one or more functions characteristic of a FATP, and various methods. The methods include those for identifying agents that bind to anFATP and those for assessing the effect of an agent  
5 being tested for its ability to modulate fatty acid transport activity. Those agents found to inhibit fatty acid transport function can be used in compositions as anti-fungal pharmaceuticals, or can be modified for greater effectiveness as a pharmaceutical.

One aspect of the invention relates to isolated nucleic acids that encode a FATP as described herein, such as those FATPs having an amino acid sequence in Figure 45  
10 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102), and Figure 55 (SEQ ID NO:57) and nucleic acids closely related thereto as described herein.

Using the information provided herein, such as a nucleic acid sequence set forth in Figures 44A-44C (SEQ ID NO:46), Figures 46A and 46B (SEQ ID NO:48), Figure  
15 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101), and Figures 54A-54C (SEQ ID NO:56), a nucleic acid of the invention encoding a FATP polypeptide may be obtained using standard cloning and screening methods, such as those for cloning and sequencing cDNA library fragments, followed by obtaining a full length clone. For example, to obtain a nucleic acid of the invention,  
20 a library of clones of cDNA of human or other mammalian DNA can be probed with a labeled oligonucleotide, such as a radiolabeled oligonucleotide, preferably about 17 nucleotides or longer, derived from a partial sequence. Clones carrying DNA identical to that of the probe can then be distinguished using stringent (also, "high stringency") hybridization conditions. By sequencing the individual clones thus identified with  
25 sequencing primers designed from the original sequence it is then possible to extend the sequence in both directions to determine the full length sequence. Suitable techniques are described, for example, in *Current Protocols in Molecular Biology* (F.M. Ausubel et

al, eds), containing supplements through Supplement 42, 1998, John Wiley and Sons, Inc., especially chapters 5, 6 and 7.

Embodiments of the invention include isolated nucleic acid molecules comprising any of the following nucleotide sequences: 1.) a nucleotide sequence which  
5 encodes a protein comprising the amino acid sequence of hsFATP1 (SEQ ID NO:47), the amino acid sequence of hsFATP2 (SEQ ID NO:49), the amino acid sequence of hsFATP3 (SEQ ID NO:51), the amino acid sequence of hsFATP4 (SEQ ID NO: 53), the amino acid sequence of hsFATP5 (SEQ ID NO:102) or the amino acid sequence of hsFATP6 (SEQ ID NO:57); 2.) nucleotide sequences of hsFATP1, hsFATP2,  
10 hsFATP3, hsFATP4, hsFATP5, or hsFATP6 (SEQ ID NO:46, 48, 50, 52, 101, or 56, respectively); 3.) a nucleotide sequence which is complementary to the nucleotide sequence of hsFATP1 (SEQ ID NO:46), hsFATP2 (SEQ ID NO:48), hsFATP3 (SEQ ID NO:50), hsFATP4 (SEQ ID NO:52), hsFATP5 (SEQ ID NO:101) or hsFATP6 (SEQ ID NO:56); 4.) a nucleotide sequence which consists of the coding region of hsFATP1  
15 (SEQ ID NO:46), the coding region of hsFATP2 (SEQ ID NO:48), the coding region of hsFATP3 (SEQ ID NO:50), the coding region of hsFATP4 (SEQ ID NO:52), the coding region of hsFATP5 (SEQ ID NO:101), or the coding region of hsFATP6 (SEQ ID NO:56).

The invention further relates to nucleic acids (nucleic acid molecules or  
20 polynucleotides) having nucleotide sequences identical over their entire length to those shown in the figures, for instance Figures 44A-44C (SEQ ID NO:46), Figures 46A and 46B (SEQ ID NO:48), Figure 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101), and Figures 54A-54C (SEQ ID NO:56). It further relates to DNA, which due to the degeneracy of the genetic code, encodes a  
25 FATP encoded by one of the FATP-encoding DNAs, whose amino acid sequence is provided herein. Also provided by the invention are nucleic acids having the coding sequences for the mature polypeptides or fragments in reading frame with other coding sequences, such as those encoding a leader or secretory sequence, a pre-, or pro- or

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prepro- protein sequence. The nucleic acids of the invention encompass nucleic acids that include a single continuous region or discontinuous regions encoding the polypeptide, together with additional regions, that may also contain coding or non-coding sequences. The nucleic acids may also contain non-coding sequences, including, 5 for example, but not limited to, non-coding 5' and 3' sequences, such as the transcribed, non-translated sequences, termination signals, ribosome binding sites, sequences that stabilize mRNA, introns, polyadenylation signals, and additional coding sequences which encode additional amino acids. For example, a marker sequence that facilitates purification of the fused polypeptide can be encoded. In certain embodiments of the 10 invention, the marker sequence can be a hexa-histidine peptide, as provided in the pQE vector (Qiagen, Inc.) and described in Gentz *et al.*, *Proc. Natl. Acad. Sci. USA* 86: 821-824 (1989), or an HA tag (Wilson *et al.*, *Cell* 37: 767 (1984)), or a sequence encoding glutathione S-transferase of *Schistosoma japonicum* (vectors available from Pharmacia; see Smith, D.B. and Johnson K.S., *Gene* 67:31 (1988) and Kaelin, W.G. *et al.*, *Cell* 15 70:351 (1992)). Nucleic acids of the invention also include, but are not limited to, nucleic acids comprising a structural gene and its naturally associated sequences that control gene expression.

The invention further relates to variants, including naturally-occurring allelic variants, of those nucleic acids described specifically herein by DNA sequence, that 20 encode variants of such polypeptides as those having the amino acid sequences shown in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53) Figures 94A and 94B (SEQ ID NO:102), or Figure 55 (SEQ ID NO:57). Such variants include nucleic acids encoding variants of the above-listed amino acid sequences, wherein those variants have several, such as 5 to 10, 1 to 5, or 3, 25 2 or 1 amino acids substituted, deleted, or added, in any combination. Variants include polynucleotides encoding polypeptides with at least 95% but less than 100% amino acid sequence identity to the polypeptides described herein by amino acid sequence. Variant polynucleotides hybridize, under low to high stringency conditions, to the alleles

described herein by DNA sequence. In one embodiment, variants have silent substitutions, additions and deletions that do not alter the properties and activities of the FATP. Allelic variants of the polynucleotides encoding hsFATP1 (Figure 45; SEQ ID NO:47), hsFATP2 (Figure 47; SEQ ID NO:49), hsFATP3 (Figure 49; SEQ ID NO:51),  
5 hsFATP4 (Figure 51; SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102) and hsFATP6 (Figure 55; SEQ ID NO:57) will be identified as mapping to chromosomal locations listed for the corresponding wild type genes in Table 2 in Example 1.

Orthologous genes are gene loci in different species that are sufficiently similar to each other in their nucleotide sequences to suggest that they originated from a  
10 common ancestral gene. Orthologous genes arise when a lineage splits into two species, rather than when a gene is duplicated within a genome. Proteins that are orthologs are encoded by genes of two different species, wherein the genes are said to be orthologous.

The invention further relates to polynucleotides encoding polypeptides which are orthologous to those polypeptides having a specific amino acid sequence described  
15 herein, such as the amino acid sequences shown in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102), or Figure 55 (SEQ ID NO:57). These polynucleotides, which can be called ortholog polynucleotides, encode orthologous polypeptides that can range in amino acid sequence identity to a reference amino acid sequence described  
20 herein, from about 65% to less than 100%, but preferably 70% to 80%, more preferably 80% to 90%, and still more preferably 90% to less than 100%. Orthologous polypeptides can also be those polypeptides that range in amino acid sequence similarity to a reference amino acid sequence described herein from about 75% to 100%, within the signature sequence. The amino acid sequence similarity between the signature  
25 sequences of orthologous polypeptides is preferably 80%, more preferably 90%, and still more preferably, 95%. The ortholog polynucleotides encode polypeptides that have similar functional characteristics (e.g., fatty acid transport activity) and similar tissue

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distribution, as appropriate to the organism from which the ortholog polynucleotides can be isolated.

Ortholog polynucleotides can be isolated from (e.g., by cloning or nucleic acid amplification methods) a great number of species, as shown by the sample of FATPs  
5 from evolutionarily divergent species described herein (see, e.g., Figures 44A-C through Figure 89). Ortholog polynucleotides corresponding to those in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102) and Figure 55 (SEQ ID NO:57) are those which can be isolated from mammals such as rat, dog, chimpanzee, monkey,  
10 baboon, pig, rabbit and guinea pig, for example.

Further variants that are fragments of the nucleic acids of the invention may be used to synthesize full-length nucleic acids of the invention, such as by use as primers in a polymerase chain reaction. As used herein, the term primer refers to a single-stranded oligonucleotide which acts as a point of initiation of template-directed DNA synthesis  
15 under appropriate conditions (e.g., in the presence of four different nucleoside triphosphates and an agent for polymerization, such as DNA or RNA polymerase or reverse transcriptase) in an appropriate buffer and at a suitable temperature. The appropriate length of a primer depends on the intended use of the primer, but typically ranges from 15 to 30 nucleotides. Short primer molecules generally require cooler  
20 temperatures to form sufficiently stable hybrid complexes with the template. A primer need not reflect the exact sequence of the template, but must be sufficiently complementary to hybridize with a template. The term primer site refers to the area of the target DNA to which a primer hybridizes. The term primer pair refers to a set of primers including a 5' (upstream) primer that hybridizes with the 5' end of the DNA  
25 sequence to be amplified and a 3' (downstream) primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

Further embodiments of the invention are nucleic acids that are at least 80% identical over their entire length to a nucleic acid described herein, for example a



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nucleic acid having the nucleotide sequence in Figures 44A-44C (SEQ ID NO:46), Figures 46A-46B (SEQ ID NO:48), Figure 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101), and Figures 54A-54C (SEQ ID NO:56). Additional embodiments are nucleic acids, and the complements of such  
5 nucleic acids, having at least 90% nucleotide sequence identity to the above-described sequences, and nucleic acids having at least 95% nucleotide sequence identity. In preferred embodiments, DNA of the present invention has 97% nucleotide sequence identity, 98% nucleotide sequence identity, or at least 99% nucleotide sequence identity with the DNA whose sequences are presented herein.

10 Other embodiments of the invention are nucleic acids that are at least 80% identical in nucleotide sequence to a nucleic acid encoding a polypeptide having an amino acid sequence as set forth in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102) or Figure 55 (SEQ ID NO:57), or as such amino acid sequences are  
15 set forth elsewhere herein, and nucleic acids that are complementary to such nucleic acids. Specific embodiments are nucleic acids having at least 90% nucleotide sequence identity to a nucleic acid encoding a polypeptide having an amino acid sequence as described in the list above, nucleic acids having at least 95% sequence identity, and nucleic acids having at least 97% sequence identity.

20 The terms "complementary" or "complementarity" as used herein, refer to the natural binding of polynucleotides under permissive salt and temperature conditions by base-pairing. Complementarity between two single-stranded molecules may be "partial" in which only some of the nucleic acids bind, or it may be complete when total complementarity exists between the single-stranded molecules (that is, when A-T and  
25 G-C base pairing is 100% complete). The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of hybridization between nucleic acid strands. This is of particular importance in amplification reactions, which depend on binding between nucleic acid strands.

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The invention further includes nucleic acids that hybridize to the above-described nucleic acids, especially those nucleic acids that hybridize under stringent hybridization conditions. "Stringent hybridization conditions" or "high stringency conditions" generally occur within a range from about  $T_m$  minus 5°C (5° C below the strand dissociation temperature or melting temperature ( $T_m$ ) of the probe nucleic acid molecule) to about 20° C to 25° C below  $T_m$ . As will be understood by those of skill in the art, the stringency of hybridization may be altered in order to identify or detect molecules having identical or related polynucleotide sequences. An example of high stringency hybridization follows. Hybridization solution is (6x SSC/10 mM

10 EDTA/0.5% SDS/5x Denhardt's solution/100 µg/ml sheared and denatured salmon sperm DNA). Hybridization is at 64-65°C for 16 hours. The hybridized blot is washed two times with 2x SSC/0.5% SDS solution at room temperature for 15 minutes each, and two times with 0.2x SSC/0.5% SDS at 65°C, for one hour each. Further examples of high stringency conditions can be found on pages 2.10.1-2.10.16 (see particularly

15 2.10.8-11) and pages 6.3.1-6 in *Current Protocols in Molecular Biology* (Ausubel, F.M. *et al.*, eds., containing supplements up through Supplement 42, 1998). Examples of high, medium, and low stringency conditions can be found on pages 36 and 37 of WO 98/40404, which are incorporated herein by reference.

The invention further relates to nucleic acids obtainable by screening an

20 appropriate library with a probe having a nucleotide sequence such as that set forth in Figures 44A-44C (SEQ ID NO:46), Figures 46A-46B (SEQ ID NO:48), Figure 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101) or Figures 54A-54C (SEQ ID NO:56), or a probe which is a sufficiently long fragment of any of the above; and isolating the nucleic acid. Such probes generally can

25 comprise at least 15 nucleotides. Nucleic acids obtainable by such screenings may include RNAs, cDNAs and genomic DNA, for example, encoding FATPs of the FATP family described herein.

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Further uses for the nucleic acid molecules of the invention, whether encoding a full-length FATP or whether comprising a contiguous portion of a nucleic acid molecule such as one given in SEQ ID NO:46, 48, 50, 52, 101, or 56, include use as markers for tissues in which the corresponding protein is preferentially expressed (to identify

5 constitutively expressed proteins or proteins produced at a particular stage of tissue differentiation or stage of development of a disease state); as molecular weight markers on southern gels; as chromosome markers or tags (when labeled, for example with biotin, a radioactive label or a fluorescent label) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in a mammal to

10 identify potential genetic disorders; as probes to hybridize and thus identify, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel nucleic acid molecules; for selecting and making oligomers for attachment to a "gene chip" or other support, to be used, for example, for examination

15 of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or to elicit another immune response.

Further methods to obtain nucleic acids encoding FATPs of the FATP family include PCR and variations thereof (e.g., "RACE" PCR and semi-specific PCR

20 methods). Portions of the nucleic acids having a nucleotide sequence set forth in Figures 44A-44C (SEQ ID NO:46), Figures 46A-46B (SEQ ID NO:48), Figure 48 (SEQ ID NO:50), Figures 50A-50C (SEQ ID NO:52), Figures 94A and 94B (SEQ ID NO:101) or Figures 54A-54C (SEQ ID NO:56), (especially "flanking sequences" on either side of a coding region) can be used as primers in methods using the polymerase

25 chain reaction, to produce DNA from an appropriate template nucleic acid.

Once a fragment of the FATP gene is generated by PCR, it can be sequenced, and the sequence of the product can be compared to other DNA sequences, for example, by using the BLAST Network Service at the National Center for Biotechnology

Information. The boundaries of the open reading frame can then be identified using semi-specific PCR or other suitable methods such as library screening. Once the 5' initiator methionine codon and the 3' stop codon have been identified, a PCR product encoding the full-length gene can be generated using genomic DNA as a template, with  
5 primers complementary to the extreme 5' and 3' ends of the gene or to their flanking sequences. The full-length genes can then be cloned into expression vectors for the production of functional proteins.

The invention also relates to isolated proteins or polypeptides such as those encoded by nucleic acids of the present invention. Isolated proteins can be purified  
10 from a natural source or can be made recombinantly. Proteins or polypeptides referred to herein as "isolated" are proteins or polypeptides that exist in a state different from the state in which they exist in cells in which they are normally expressed in an organism, and include proteins or polypeptides obtained by methods described herein, similar methods or other suitable methods, and also include essentially pure proteins or  
15 polypeptides, proteins or polypeptides produced by chemical synthesis or by combinations of biological and chemical methods, and recombinant proteins or polypeptides which are isolated. Thus, the term "isolated" as used herein, indicates that the polypeptide in question exists in a physical milieu distinct from that in which it occurs in nature. Thus, "isolated" includes existing in membrane fragments and vesicles  
20 membrane fractions, liposomes, lipid bilayers and other artificial membrane systems. An isolated FATP may be substantially isolated with respect to the complex cellular milieu in which it naturally occurs, and may even be purified essentially to homogeneity, for example as determined by PAGE or column chromatography (for example, HPLC), but may also have further cofactors or molecular stabilizers, such as  
25 detergents, added to the purified protein to enhance activity. In one embodiment, proteins or polypeptides are isolated to a state at least about 75% pure; more preferably at least about 85% pure, and still more preferably at least about 95% pure, as determined by Coomassie blue staining of proteins on SDS-polyacrylamide gels. Proteins or

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polypeptides referred to herein as "recombinant" are proteins or polypeptides produced by the expression of recombinant nucleic acids.

In a preferred embodiment, an isolated polypeptide comprising a FATP, a functional portion thereof, or a functional equivalent of the FATP, has at least one function characteristic of a FATP, for example, transport activity, binding function (e.g., a domain which binds to AMP), or antigenic function (e.g., binding of antibodies that also bind to a naturally-occurring FATP, as that function is found in an antigenic determinant). Functional equivalents can have activities that are quantitatively similar to, greater than, or less than, the reference protein. These proteins include, for example, naturally occurring FATPs that can be purified from tissues in which they are produced (including polymorphic or allelic variants), variants (e.g., mutants) of those proteins and/or portions thereof. Such variants include mutants differing by the addition, deletion or substitution of one or more amino acid residues, or modified polypeptides in which one or more residues are modified, and mutants comprising one or more modified residues. Portions or fragments of a FATP can range in size from four amino acid residues to the entire amino acid sequence minus one amino acid.

The isolated proteins of the invention preferably include mammalian fatty acid transport proteins of the FATP family of homologous proteins. In one embodiment, the extent of amino acid sequence similarity between a polypeptide having one of the amino acid sequences shown in Figure 45 (SEQ ID NO:47), Figure 47 (SEQ ID NO:49), Figure 49 (SEQ ID NO:51), Figure 51 (SEQ ID NO:53), Figures 94A and 94B (SEQ ID NO:102), or Figure 55 (SEQ ID NO:57), and the respective functional equivalents of these polypeptides is at least about 88%. In other embodiments, the degree of amino acid sequence similarity between a FATP and its respective functional equivalent is at least about 91%, at least about 94%, or at least about 97%.

The polypeptides of the invention also include those FATPs encoded by polynucleotides which are orthologous to those polynucleotides, the sequences of which are described herein in whole or in part. FATPs which are orthologs to those described

herein by amino acid sequence, in whole or in part, are, for example fatty acid transport proteins 1-6 of dog, rat chimpanzee, monkey, rabbit, guinea pig, baboon and pig, and are also embodiments of the invention.

To determine the percent identity or similarity of two amino acid sequences or  
5 of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment, and non-homologous (dissimilar) sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%,  
10 preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, and even more preferably at least 70%, 80%, or 90% of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding  
15 position in the second sequence, then the molecules are identical at that position (as used herein, amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "similarity"). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment  
20 of the two sequences.

The invention also encompasses polypeptides having a lower degree of identity but having sufficient similarity so as to perform one or more of the same functions performed by the polypeptides described herein by amino acid sequence. Similarity for a polypeptide is determined by conserved amino acid substitution. Such substitutions  
25 are those that substitute a given amino acid in a polypeptide by another amino acid of like characteristics. Conservative substitutions are likely to be phenotypically silent. Typically seen as conservative substitutions are the replacements, one for another, among the aliphatic amino acids Ala, Val, Leu, and Ile; interchange of the hydroxyl

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residues Ser and Thr, exchange of the acidic residues Asp and Glu, substitution between the amide residues Asn and Gln, exchange of the basic residues Lys and Arg and replacements among the aromatic residues Phe, Tyr. Guidance concerning which amino acid changes are likely to be phenotypically silent is found in Bowie *et al.*, *Science* 5 247:1306-1310 (1990).

TABLE 1. Conservative Amino Acid Substitutions

	Aromatic		Phenylalanine	
			Tryptophan	
			Tyrosine	
	Hydrophobic		Leucine	
			Isoleucine	
			Valine	
	Polar		Glutamine	
			Asparagine	
5	Basic		Arginine	
			Lysine	
			Histidine	
	Acidic		Aspartic Acid	
			Glutamic Acid	
	Small		Alanine	
			Serine	
			Threonine	
			Methionine	
			Glycine	

The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm.

- 10 (Computational Molecular Biology, Lesk, A.M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D.W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part 1, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; Sequence



*Analysis in Molecular Biology*, von Heinje, G., Academic Press, 1987; and *Sequence Analysis Primer*, Gribskov, M. and Devereaux, J., eds., M. Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* 5 (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at <http://www.gcg.com>), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the 10 GCG software package (Devereux, J., *et al.*, *Nucleic Acids Res.* 12(1):387 (1984)) (available at <http://www.gcg.com>), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Meyers and W. Miller (*CABIOS*, 4:11-17 (1989)) 15 which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against databases to, for example, identify other family members or related sequences. Such searches can be performed 20 using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (*J. Mol. Biol.* 215:403-10 (1990)). BLAST nucleotide searches can be performed with the NBLAST program, score = 100, word length = 12 to obtain nucleotide sequences homologous to (with calculatably significant similarity to) the nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, 25 score = 50, word length = 3 to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (*Nucleic Acids Res.* 25(17):3389-3402 (1997)). When utilizing BLAST and gapped BLAST programs, the default

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parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>.

Similarity for nucleotide and amino acid sequences can be defined in terms of the parameters set by the Advanced Blast search available from NCBI (the National Center for Biotechnology Information; see, for Advanced BLAST page, [www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast?Jform=1](http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast?Jform=1)). These default parameters, recommended for a query molecule of length greater than 85 amino acid residues or nucleotides have been set as follows: gap existence cost, 11, per residue gap cost, 1; lambda ratio, 0.85. Further explanation of version 2.0 of BLAST can be found on related website pages and in Altschul, S.F. *et al.*, *Nucleic Acids Res.* 25:3389-3402 (1997).

The invention further relates to fusion proteins, comprising a FATP or functional portion thereof (as described above) as a first moiety, linked to second moiety not occurring in the FATP as found in nature. Thus, the second moiety can be an amino acid, peptide or polypeptide. The first moiety can be in an N-terminal location, C-terminal location or internal to the fusion protein. In one embodiment, the fusion protein comprises a FATP as the first moiety, and a second moiety comprising a linker sequence and an affinity ligand. Fusion proteins can be produced by a variety of methods. For example, a fusion protein can be produced by the insertion of a FATP gene or portion thereof into a suitable expression vector, such as Bluescript SK +/- (Stratagene), pGEX-4T-2 (Pharmacia), pET-24(+) (Novagen), or vectors of similar construction. The resulting construct can be introduced into a suitable host cell for expression. Upon expression, fusion protein can be purified from cells by means of a suitable affinity matrix (See e.g., *Current Protocols in Molecular Biology*, Ausubel, F.M. *et al.*, eds., Vol. 2, pp. 16.4.1-16.7.8, containing supplements up through Supplement 42, 1998).

The invention also relates to enzymatically produced, synthetically produced, or recombinantly produced portions of a fatty acid transport protein. Portions of a FATP

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can be made which have full or partial function on their own, or which when mixed together (though fully, partially, or nonfunctional alone), spontaneously assemble with one or more other polypeptides to reconstitute a functional protein having at least one function characteristic of a FATP.

5           Fragments of a FATP can be produced by direct peptide synthesis, for example those using solid-phase techniques (Roberge, J.Y. *et al.*, *Science* 269:202-204 (1995); Merrifield, J., *J. Am. Chem. Soc.* 85:2149-2154 (1963)). Protein synthesis can be performed using manual techniques or by automation. Automated synthesis can be carried out using, for instance, an Applied Biosystems 431A Peptide Synthesizer  
10           (Perkin Elmer). Various fragments of a FATP can be synthesized separately and combined using chemical methods.

          One aspect of the invention is a peptide or polypeptide having the amino acid sequence of a portion of a fatty acid transport protein which is hydrophilic rather than hydrophobic, and ordinarily can be detected as facing the outside of the cell membrane.  
15           Such a peptide or polypeptide can be thought of as being an extracellular domain of the FATP, or a mimetic of said extracellular domain. It is known, for example, that a portion of human FATP4 that includes a highly conserved motif is involved in AMP-CoA binding function (Stuhlsatz-Krouper, S.M. *et al.*, *J. Biol. Chem.* 44:28642-28650 (1998)).

20           The term "mimetic" as used herein, refers to a molecule, the structure of which is developed from knowledge of the structure of the FATP of interest, or one or more portions thereof, and, as such, is able to effect some or all of the functions of a FATP.

          Portions of an FATP can be prepared by enzymatic cleavage of the isolated protein, or can be made by chemical synthesis methods. Portions of a FATP can also be  
25           made by recombinant DNA methods in which restriction fragments, or fragments that may have undergone further enzymatic processing, or synthetically made DNAs are joined together to construct an altered FATP gene. The gene can be made such that it encodes one or more desired portions of a FATP. These portions of FATP can be

entirely homologous to a known FATP, or can be altered in amino acid sequence relative to naturally occurring FATPs to enhance or introduce desired properties such as solubility, stability, or affinity to a ligand. A further feature of the gene can be a sequence encoding an N-terminal signal peptide directed to the plasma membrane.

5           An extracellular domain can be determined by a hydrophobicity plot, such as those shown in Figures 28A, 29A, and 35A, or by a hydrophilicity plot such as those shown in Figures 28C, 29C, 35C, 91, 92 and 93. A polypeptide or peptide comprising all or a portion of a FATP extracellular domain can be used in a pharmaceutical composition. When administered to a mammal by an appropriate route, the polypeptide  
10 or peptide can bind to fatty acids and compete with the native FATPs in the membrane of cells, thereby making fewer fatty acid molecules available as substrates for transport into cells, and reducing the amount of fatty acids taken up by, for example, the heart, in the case of FATP6.

          Another aspect of the invention relates to a method of producing a fatty acid  
15 transport protein, variants or portions thereof, and to expression systems and host cells containing a vector appropriate for expression of a fatty acid transport protein.

          Cells that express a FATP, a variant or a portion thereof, or an ortholog of a FATP described herein by amino acid sequence, can be made and maintained in culture, under conditions suitable for expression, to produce protein in the cells for cell-based  
20 assays, or to produce protein for isolation. These cells can be procaryotic or eucaryotic. Examples of procaryotic cells that can be used for expression include *Escherichia coli*, *Bacillus subtilis* and other bacteria. Examples of eucaryotic cells that can be used for expression include yeasts such as *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Pichia pastoris* and other lower eucaryotic cells, and cells of higher eucaryotes  
25 such as those from insects and mammals, such as primary cells and cell lines such as CHO, HeLa, 3T3 and BHK cells, preferably COS cells and human kidney 293 cells, and more preferably Jurkat cells. (See, e.g., Ausubel, F.M. *et al.*, eds. *Current Protocols in*

*Molecular Biology*, Greene Publishing Associates and John Wiley & Sons, Inc., containing Supplements up through Supplement 42, 1998)).

In one embodiment, host cells that produce a recombinant FATP, or a portion thereof, a variant, or an ortholog of a FATP described herein by amino acid sequence, can be made as follows. A gene encoding a FATP, variant or a portion thereof can be inserted into a nucleic acid vector, e.g., a DNA vector, such as a plasmid, phage, cosmid, phagemid, virus, virus-derived vector (e.g., SV40, vaccinia, adenovirus, fowl pox virus, pseudorabies viruses, retroviruses) or other suitable replicon, which can be present in a single copy or multiple copies, or the gene can be integrated in a host cell chromosome. A suitable replicon or integrated gene can contain all or part of the coding sequence for a FATP or variant, operably linked to one or more expression control regions whereby the coding sequence is under the control of transcription signals and linked to appropriate translation signals to permit translation. The vector can be introduced into cells by a method appropriate to the type of host cells (e.g., transfection, electroporation, infection). For expression from the FATP gene, the host cells can be maintained under appropriate conditions (e.g., in the presence of inducer, normal growth conditions, etc.). Proteins or polypeptides thus produced can be recovered (e.g., from the cells, as in a membrane fraction, from the periplasmic space of bacteria, from culture medium) using suitable techniques. Appropriate membrane targeting signals may be incorporated into the expressed polypeptide. These signals may be endogenous to the polypeptide or they may be heterologous signals.

Polypeptides of the invention can be recovered and purified from cell cultures (or from their primary cell source) by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and high performance liquid chromatography. Known methods for refolding protein can be used to regenerate active conformation if the polypeptide is denatured during isolation or purification.

In a further aspect of the invention are methods for assessing the transport function of any of the fatty acid transport proteins or polypeptides described herein, including orthologs, and in variations of these, methods for identifying an inhibitor (or an enhancer) of such function and methods for assessing the transport function in the presence of a candidate inhibitor or a known inhibitor.

A variety of systems comprising living cells can be used for these methods. Cells to be used in fatty acid transport assays, and further in methods for identifying an inhibitor or enhancer of this function, express one or more FATPs. See Examples 3, 6, 9, 12 and 14 for data on tissue distribution of expression of FATPs, and Examples 10 and 11 describing recombinant cells expressing FATP. Cells for use in cell-based assays described herein can be drawn from a variety of sources, such as isolated primary cells of various organs and tissues wherein one or more FATPs are naturally expressed. In some cases, the cells can be from adult organs, and in some cases, from embryonic or fetal organs, such as heart, lung, liver, intestine, skeletal muscle, kidney and the like. Cells for this purpose can also include cells cultured as fragments of organs or in conditions simulating the cell type and/or tissue organization of organs, in which artificial materials may be used as substrates for cell growth. Other types of cells suitable for this purpose include cells of a cell strain or cell line (ordinarily comprising cells considered to be "transformed") transfected to express one or more FATPs.

A further embodiment of the invention is a method for detecting, in a sample of cells, a fatty acid transport protein, a portion or fragment thereof, a fusion protein comprising a FATP or a portion thereof, or an ortholog as described herein, wherein the cells can be, for instance, cells of a tissue, primary culture cells, or cells of a cell line, including cells into which nucleic acid has been introduced. The method comprises adding to the sample an agent that specifically binds to the protein, and detecting the agent specifically bound to the protein. Appropriate washing steps can be added to reduce nonspecific binding to the agent. The agent can be, for example, an antibody, a ligand or a substrate mimic. The agent can have incorporated into it, or have bound to

it, covalently or by high affinity non-covalent interactions, for instance, a label that facilitates detection of the agent to which it is bound, wherein the label can be, but is not limited to, a phosphorescent label, a fluorescent label, a biotin or avidin label, or a radioactive label. The means of detection of a fatty acid transport protein can vary, as  
5 appropriate to the agent and label used. For example, for an antibody that binds to the fatty acid transport protein, the means of detection may call for binding a second antibody, which has been conjugated to an enzyme, to the antibody which binds the fatty acid transport protein, and detecting the presence of the second antibody by means of the enzymatic activity of the conjugated enzyme.

10 Similar principles can also be applied to a cell lysate or a more purified preparation of proteins from cells that may comprise a fatty acid transport protein of interest, for example in the methods of immunoprecipitation, immunoblotting, immunoaffinity methods, that in addition to detection of the particular FATP, can also be used in purification steps, and qualitative and quantitative immunoassays. See, for  
15 instance, chapters 11 through 14 in *Antibodies: A Laboratory Manual*, E. Harlow and D. Lane, eds., Cold Spring Harbor Laboratory, 1988.

Isolated fatty acid transport protein or, an antigenically similar portion thereof, especially a portion that is soluble, can be used in a method to select and identify molecules which bind specifically to the FATP. Fusion proteins comprising all of, or a  
20 portion of, the fatty acid transport protein linked to a second moiety not occurring in the FATP as found in nature, can be prepared for use in another embodiment of the method. Suitable fusion proteins for this purpose include those in which the second moiety comprises an affinity ligand (e.g., an enzyme, antigen, epitope). FATP fusion proteins can be produced by the insertion of a gene encoding the FATP or a variant thereof, or a  
25 suitable portion of such gene into a suitable expression vector, which encodes an affinity ligand (e.g., pGEX-4T-2 and pET-15b, encoding glutathione S-transferase and His-Tag affinity ligands, respectively). The expression vector can be introduced into a suitable host cell for expression. Host cells are lysed and the lysate, containing fusion

protein, can be bound to a suitable affinity matrix by contacting the lysate with an affinity matrix.

In one embodiment, the fusion protein can be immobilized on a suitable affinity matrix under conditions sufficient to bind the affinity ligand portion of the fusion protein to the matrix, and is contacted with one or more candidate binding agents (e.g., a mixture of peptides) to be tested, under conditions suitable for binding of the binding agents to the FATP portion of the bound fusion protein. Next, the affinity matrix with bound fusion protein can be washed with a suitable wash buffer to remove unbound candidate binding agents and non-specifically bound candidate binding agents. Those agents which remain bound can be released by contacting the affinity matrix with fusion protein bound thereto with a suitable elution buffer. Wash buffer can be formulated to permit binding of the fusion protein to the affinity matrix, without significantly disrupting binding of specifically bound binding agents. In this aspect, elution buffer can be formulated to permit retention of the fusion protein by the affinity matrix, but can be formulated to interfere with binding of the candidate binding agents to the target portion of the fusion protein. For example, a change in the ionic strength or pH of the elution buffer can lead to release of specifically bound agent, or the elution buffer can comprise a release component or components designed to disrupt binding of specifically bound agent to the target portion of the fusion protein.

Immobilization can be performed prior to, simultaneous with, or after, contacting the fusion protein with candidate binding agent, as appropriate. Various permutations of the method are possible, depending upon factors such as the candidate molecules tested, the affinity matrix-ligand pair selected, and elution buffer formulation. For example, after the wash step, fusion protein with binding agent molecules bound thereto can be eluted from the affinity matrix with a suitable elution buffer (a matrix elution buffer, such as glutathione for a GST fusion). Where the fusion protein comprises a cleavable linker, such as a thrombin cleavage site, cleavage from the affinity ligand can release a portion of the fusion with the candidate agent bound



thereto. Bound agent molecules can then be released from the fusion protein or its cleavage product by an appropriate method, such as extraction.

One or more candidate binding agents can be tested simultaneously. Where a mixture of candidate binding agents is tested, those found to bind by the foregoing processes can be separated (as appropriate) and identified by suitable methods (e.g.,  
5 PCR, sequencing, chromatography). Large libraries of candidate binding agents (e.g., peptides, RNA oligonucleotides) produced by combinatorial chemical synthesis or by other methods can be tested (see e.g., Ohlmeyer, M.H.J. *et al.*, *Proc. Natl. Acad. Sci. USA* 90:10922-10926 (1993) and DeWitt, S.H. *et al.*, *Proc. Natl. Acad. Sci. USA*  
10 90:6909-6913 (1993), relating to tagged compounds; see also Rutter, W.J. *et al.* U.S. Patent No. 5,010,175; Huebner, V.D. *et al.*, U.S. Patent No. 5,182,366; and Geysen, H.M., U.S. Patent No. 4,833,092). Random sequence RNA libraries (see Ellington, A.D. *et al.*, *Nature* 346:818-822 (1990); Bock, L.C. *et al.*, *Nature* 355:584-566 (1992); and Szostak, J.W., *Trends in Biochem. Sci.* 17:89-93 (March, 1992)) can also be  
15 screened according to the present method to select RNA molecules which bind to a target FATP or FATP fusion protein. Where binding agents selected from a combinatorial library by the present method carry unique tags, identification of individual biomolecules by chromatographic methods is possible. Where binding agents do not carry tags, chromatographic separation, followed by mass spectrometry to  
20 ascertain structure, can be used to identify binding agents selected by the method, for example.

The invention also comprises a method for identifying an agent which inhibits interaction between a fatty acid transport protein (e.g., one comprising the amino acid sequence in SEQ ID NO:47, SEQ ID NO:49, SEQ ID NO:51, SEQ ID NO:53, SEQ ID  
25 NO:102, or SEQ ID NO:57), and a ligand of said protein. The FATP can be one described by amino acid sequence herein, a portion or fragment thereof, a variant thereof, or an ortholog thereof, or a FATP fusion protein. Here, a ligand can be, for instance, a substrate, or a substrate mimic, an antibody, or a compound, such as a

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peptide, that binds with specificity to a site on the protein. The method comprises combining, not limited to a particular order, the fatty acid protein, the ligand of the protein, and a candidate agent to be assessed for its ability to inhibit interaction between the protein and the ligand, under conditions appropriate for interaction between the protein and the ligand (e.g., pH, salt, temperature conditions conducive to appropriate conformation and molecular interactions); determining the extent to which the protein and ligand interact; and comparing (1) the extent of protein-ligand interaction in the presence of candidate agent with (2) the extent of protein-ligand interaction in the absence of candidate agent, wherein if (1) is less than (2), then the candidate agent is one which inhibits interaction between the protein and the ligand.

The method can be facilitated, for example, by using an experimental system which employs a solid support (column chromatography matrix, wall of a plate, microtiter wells, column pore glass, pins to be submerged in a solution, beads, etc.) to which the protein can be attached. Accordingly, in one embodiment, the protein can be fixed to a solid phase directly or indirectly, by a linker. The candidate agent to be tested is added under conditions conducive for interaction and binding to the protein. The ligand is added to the solid phase system under conditions appropriate for binding. Excess ligand is removed, as by a series of washes done under conditions that do not disrupt protein-ligand interactions. Detection of bound ligand can be facilitated by using a ligand that carries a label (e.g., fluorescent, chemiluminescent, radioactive). In a control experiment, protein and ligand are allowed to interact in the absence of any candidate agent, under conditions otherwise identical to those used for the "test" conditions where candidate inhibiting agent is present, and any washes used in the test conditions are also used in the control. The extent to which ligand binds to the protein in the presence of candidate agent is compared to the extent to which ligand binds to the protein in the absence of the candidate agent. If the extent to which interaction of the protein and the ligand occurs is less in the presence of the candidate agent than in the

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absence of the candidate agent, the candidate agent is an agent which inhibits interaction between the protein and the ligand of the protein.

In a further embodiment, an inhibitor (or an enhancer) of a fatty acid transport protein can be identified. The method comprises steps which are, or are variations of the following: contacting the cells with fatty acid, wherein the fatty acid can be labeled  
5 for convenience of detection; contacting a first aliquot of the cells with an agent being tested as an inhibitor (or enhancer) of fatty acid uptake while maintaining a second aliquot of cells under the same conditions but without contact with the agent; and measuring (e.g., quantitating) fatty acid in the first and second aliquots of cells; wherein  
10 a lesser quantity of fatty acid in the first aliquot compared to that in the second aliquot is indicative that the agent is an inhibitor of fatty acid uptake by a fatty acid transport protein. A greater quantity of fatty acid in the first aliquot compared to that in the second aliquot is indicative that the agent is an enhancer of fatty acid uptake by a fatty acid transport protein.

15 A particular embodiment of identifying an inhibitor or enhancer of fatty acid transport function employs the above steps, but also employs additional steps preceding those given above: introducing into cells of a cell strain or cell line ("host cells" for the intended introduction of, or after the introduction of, a vector) a vector comprising a fatty acid transport protein gene, wherein expression of the gene can be regulatable or  
20 constitutive, and providing conditions to the host cells under which expression of the gene can occur.

The terms "contacting" and "combining" as used herein in the context of bringing molecules into close proximity to each other, can be accomplished by conventional means. For example, when referring to molecules that are soluble,  
25 contacting is achieved by adding the molecules together in a solution. "Contacting" can also be adding an agent to a test system, such as a vessel containing cells in tissue culture.

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The term "inhibitor" or "antagonist", as used herein, refers to an agent which blocks, diminishes, inhibits, hinders, limits, decreases, reduces, restricts or interferes with fatty acid transport into the cytoplasm of a cell, or alternatively and additionally, prevents or impedes the cellular effects associated with fatty acid transport. The term  
5 "enhancer" or "agonist", as used herein, refers to an agent which augments, enhances, or increases fatty acid transport into the cytoplasm of a cell. An antagonist will decrease fatty acid concentration, fatty acid metabolism and byproduct levels in the cell, leading to phenotypic and molecular changes.

In order to produce a "host cell" type suitable for fatty acid uptake assays and for  
10 assays derived therefrom for identifying inhibitors or enhancers thereof, a nucleic acid vector can be constructed to comprise a gene encoding a fatty acid transport protein, for example, human FATP1, FATP2, FATP3, FATP4, FATP5, FATP6, a mutant or variant thereof, an ortholog of the human proteins, such as mouse orthologs or orthologs found in other mammals, or a FATP family protein of origin in an organism other than a  
15 mammal. The gene of the vector can be regulatable, such as by the placement of the gene under the control of an inducible or repressible promoter in the vector (e.g., inducible or repressible by a change in growth conditions of the host cell harboring the vector, such as addition of inducer, binding or functional removal of repressor from the cell milieu, or change in temperature) such that expression of the FATP gene can be  
20 turned on or initiated by causing a change in growth conditions, thereby causing the protein encoded by the gene to be produced, in host cells comprising the vector, as a plasma membrane protein. Alternatively, the FATP gene can be constitutively expressed.

A vector comprising an FATP gene, such as a vector described herein, can be  
25 introduced into host cells by a means appropriate to the vector and to the host cell type. For example, commonly used methods such as electroporation, transfection, for instance, transfection using  $\text{CaCl}_2$ , and transduction (as for a virus or bacteriophage) can be used. Host cells can be, for example, mammalian cells such as primary culture cells

or cells of cell lines such as COS cells, 293 cells or Jurkat cells. Host cells can also be, in some cases, cells derived from insects, cells of insect cell lines, bacterial cells, such as *E. coli*, or yeast cells, such as *S. cerevisiae*. It is preferred that the fatty acid transport protein whose function is to be assessed, with or without a candidate inhibitor or  
5 enhancer, be produced in host cells whose ancestor cells originated in a species related to the species of origin of the FATP gene encoding the fatty acid transport protein. For example, it is preferable that tests of function or of inhibition or enhancement of a mammalian FATP be carried out in host mammalian cells producing the FATP, rather than bacterial cells or yeast cells.

10 Host cells comprising a vector comprising a regulatable FATP gene can be treated so as to allow expression of the FATP gene and production of the encoded protein (e.g., by contacting the cells with an inducer compound that effects transcription from an inducible promoter operably linked to the FATP gene).

The test agent (e.g., an agonist or antagonist) is added to the cells to be used in a  
15 fatty acid transport assay, in the presence or absence of test agent, under conditions suitable for production and/or maintenance of the expressed FATP in a conformation appropriate for association of the FATP with test agent and substrate. For example, conditions under which an agent is assessed, such as media and temperature requirements, can, initially, be similar to those necessary for transport of typical fatty  
20 acid substrates across the plasma membrane. One of ordinary skill in the art will know how to vary experimental conditions depending upon the biochemical nature of the test agent. The test agent can be added to the cells in the presence of fatty acid, or in the absence of fatty acid substrate, with the fatty acid substrate being added following the addition of the test agent. The concentration at which the test agent can be evaluated  
25 can be varied, as appropriate, to test for an increased effect with increasing concentrations.

Test agents to be assessed for their effects on fatty acid transport can be any chemical (element, molecule, compound), made synthetically, made by recombinant

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techniques or isolated from a natural source. For example, test agents can be peptides, polypeptides, peptoids, sugars, hormones, or nucleic acid molecules, such as antisense nucleic acid molecules. In addition, test agents can be small molecules or molecules of greater complexity made by combinatorial chemistry, for example, and compiled into libraries. These libraries can comprise, for example, alcohols, alkyl halides, amines, amides, esters, aldehydes, ethers and other classes of organic compounds. Test agents can also be natural or genetically engineered products isolated from lysates of cells, bacterial, animal or plant, or can be the cell lysates themselves. Presentation of test compounds to the test system can be in either an isolated form or as mixtures of compounds, especially in initial screening steps.

Thus, the invention relates to a method for identifying agents which alter fatty acid transport, the method comprising providing the test agent to the cell (wherein "cell" includes the plural, and can include cells of a cell strain, cell line or culture of primary cells or organ culture, for example), under conditions suitable for binding to its target, whether to the FATP itself or to another target on or in the cell, wherein the transformed cell comprises a FATP.

In greater detail, to test one or more agents or compounds (e.g., a mixture of compounds can conveniently be screened initially) for inhibition of the transport function of a fatty acid transport protein, the agent(s) can be contacted with the cells. The cells can be contacted with a labeled fatty acid. The fatty acid can be, for example, a known substrate of the fatty acid transport protein such as oleate or palmitate. The fatty acid can itself be labeled with a radioactive isotope, (e.g.,  $^3\text{H}$  or  $^{14}\text{C}$ ) or can have a radioactively labeled adduct attached. In other variations, the fatty acid can have chemically attached to it a fluorescent label, or a substrate for an enzyme occurring within the cells, wherein the substrate yields a detectable product, such as a highly colored or fluorescent product. Addition of candidate inhibitors and labeled substrate to the cells comprising fatty acid transport protein can be in either order or can be simultaneous.

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A second aliquot of cells, which can be called "control" cells (a "first" aliquot of cells can be called "test" cells), is treated, if necessary (as in the case of transformed "host" cells), so as to allow expression of the FATP gene, and is contacted with the labeled substrate of the fatty acid transport protein. The second aliquot of cells is not  
5 contacted with one or more agents to be tested for inhibition of the transport function of the protein produced in the cells, but is otherwise kept under the same culture conditions as the first aliquot of cells.

In a further step of a method to identify inhibitors of a fatty acid transport protein, the labeled fatty acid is measured in the first and second aliquots of cells. A  
10 preliminary step of this measurement process can be to separate the external medium from the cells so as to be able to distinguish the labeled fatty acid external to the cells from that which has been transported inside the cells. This can be accomplished, for instance, by removing the cells from their growth container, centrifuging the cell suspension, removing the supernatant and performing one or more wash steps to  
15 extensively dilute the remaining medium which may contain labeled fatty acid. Detection of the labeled fatty acid can be by a means appropriate to the label used. For example, for a radioactive label, detection can be by scintillation counting of appropriately prepared samples of cells (e.g., lysates or protein extracts); for a fluorescent label, by measuring fluorescence in the cells by appropriate instrumentation.

20 If a compound tested as a candidate inhibitor of transport function causes the test cells to have less labeled fatty acid detected in the cells than that detected in the control cells, then the compound is an inhibitor of the fatty acid transport protein. Procedures analogous to those above can be devised for identifying enhancers (agonists of FATPs) of fatty acid transport function wherein if the test cells contain more labeled fatty acid  
25 than that detected in the control cells, or if the fatty acid is taken up at a higher rate, then the compound being tested can be concluded to be an enhancer of the fatty acid transport protein.

Example 13 describes use of an assay of this type to identify an inhibitor of a FATP. In Example 13, an antisense oligonucleotide which specifically inhibits biosynthesis of mmFATP4 was demonstrated to inhibit fatty acid uptake into mouse enterocytes. Similarly, antisense oligonucleotides directed towards specifically  
5 inhibiting the biosynthesis of FATP6 in heart cells, FATP5 in liver cells, FATP3 in lung cells, and FATP2 in colon cells, can be demonstrated as examples of "test agents" that inhibit fatty acid transport.

Another assay to determine whether an agent is an inhibitor (or enhancer) of fatty acid transport employs animals, one or more of which are administered the agent,  
10 and one or more of which are maintained under similar conditions, but are not administered the agent. Both groups of animals are given fatty acids (e.g., orally, intravenously, by tube inserted into stomach or intestine), and the fatty acids taken up into a bodily fluid (e.g., serum) or into an organ or tissue of interest are measured from comparable samples taken from each group of animals. The fatty acids may carry a  
15 label (e.g., radioactive) to facilitate detection and quantitation of fatty acids taken up into the fluid or tissue being sampled. This type of assay can be used alone or can be used in addition to *in vitro* assays of a candidate inhibitor or enhancer.

An agent determined to be an inhibitor (or enhancer) of FATP function, such as fatty acid binding and/or fatty acid uptake, can be administered to cells in culture, or *in vivo*, to a mammal (e.g. human) to inhibit (or enhance) FATP function. Such an agent  
20 may be one that acts directly on the FATP (for example, by binding) or can act on an intermediate in a biosynthetic pathway to produce FATP, such as transcription of the FATP gene, processing of the mRNA, or translation of the mRNA. An example of such an agent is antisense oligonucleotide.

25 Antisense methods similar to those illustrated in Example 13 can be used to determine the target FATP of a compound or agent that has an inhibitory or enhancing effect on fatty acid uptake. For example, antisense oligonucleotide directed to the inhibition of FATP4 biosynthesis can be added to lung cells or cell lines derived from



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lung cells. In addition, antisense oligonucleotides directed to the inhibition of other FATPs, except for FATP3, can also be added to the lung cells. The administration of antisense oligonucleotides in this manner ensures that the predominant FATP activity remaining in the cells comes from FATP3. After a period of incubation of the cells with the antisense oligonucleotides sufficient to deplete the plasma membrane of the FATPs whose biosynthesis has been inhibited, a test agent, preferably one that has been shown by some preliminary test to have an inhibitory or enhancing activity on fatty acid transport, can be added to the lung cells. If the test agent is now demonstrated, after treatment of the cells with antisense oligonucleotides, to have an inhibitory or enhancing activity on fatty acid transport in the lung cells, it can be concluded that the target of the test agent is FATP3, or a molecule involved in the biosynthesis or activity of FATP3.

In another type of cell-based assay for uptake of fatty acids, a change of intracellular pH resulting from the uptake of fatty acids can be followed by an indicator fluorophore. The fluorophore can be taken up by the cells in a preincubation step. Fatty acids can be added to the cell medium, and after some period of incubation to allow FATP-mediated uptake of fatty acids, the change in  $\lambda_{\max}$  of fluorescence can be measured, as an indicator of a change in intracellular pH, as the  $\lambda_{\max}$  of fluorescence of the fluorophore changes with the pH of its environment, thereby indicating uptake of fatty acids. One such fluorophore is BCECF (2', 7'-bis(2-carboxyethyl)-5(6)-carboxyfluorescein; Rink, T.J. *et al.*, *J. Cell. Biol.* 95: 189 (1982)).

In assays similar to those described above, a candidate inhibitor or enhancer of fatty acid transport function can be added (or mock-added, for control cultures) to cultures of cells engineered to express a desired FATP to which fatty acid substrate is also added. Inhibition of fatty acid uptake is indicated by a lack of the drop in pH, indicating fatty acid uptake, that is seen in control cells. Enhancement of fatty acid uptake is indicated by a decrease in intracellular pH, as compared to control cells not receiving the candidate enhancer of fatty acid transport function.

Yeast cells can be used in a similar cell-based assay for the uptake of fatty acids mediated by a FATP, and such an assay can be adapted to a screening assay for the identification of agents that inhibit or enhance fatty acid uptake by an FATP. Yeast cells lacking an endogenous FATP activity (mutated, disrupted or deleted for *FAT1*;  
5 Faergeman, N.J. *et al.*, *J. Biol. Chem.* 272(13):8531-8538 (1997); Watkins, P.A. *et al.*, *J. Biol. Chem.* 273(29):18210-18219 (1998)) can be engineered to harbor a related gene of the family of FATP-encoding genes, such as a mammalian FATP (e.g., human FATP4).

Examples of expression vectors include pEG (Mitchell, D.A., *et al.*, *Yeast* 9:715-  
10 723 (1993)) and pDAD1 and pDAD2, which contain a *GAL1* promoter (Davis, L. I. and Fink, G. R., *Cell* 61:965-978 (1990)). A variety of promoters are suitable for expression. Available yeast vectors offer a choice of promoters. In one embodiment, the inducible *GAL1* promoter is used. In another embodiment, the constitutive *ADHI* promoter (alcohol dehydrogenase; Bennetzen, J. L. and Hall, B. D., *J. Biol. Chem.*  
15 257:3026-3031 (1982)) can be used to express an inserted gene on glucose-containing media. An example of a vector suitable for expression of a heterologous FATP gene in yeast is pQB169.

With the introduced FATP gene providing the only fatty acid transport protein function for the yeast cells, it is possible to study effect of the heterologous FATP on  
20 fatty acid transport into the yeast cells in isolation. Assays for the uptake of fatty acids into the yeast cells can be devised that are similar to those described above and/or those assays that have been illustrated in the Examples. Tests for candidate inhibitors or enhancers of the heterologous FATP can be done in cultures of yeast cells, wherein the yeast cells are incubated with fatty acid substrate and an agent to be tested as an  
25 inhibitor or enhancer of FATP function. FATP uptake after a period of time can be measured by analyzing the contents of the yeast cells for fatty acid substrate, as compared with control yeast cells incubated with the fatty acid, but not with the test agent. Yeast cells have the additional advantage, over mammalian cells in culture, for

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example, that yeast cells can be forced to rely upon fatty acids as their only source of carbon, if the growth medium supplied to the yeast cells is formulated to contain no other source of carbon. Thus, the effect of the heterologous FATP on fatty acid uptake and metabolism in the engineered yeast cells can be amplified. An agent that efficiently  
5 blocks transport function of the heterologous FATP could result in death of the yeast cells. Thus, in this case, inhibition of function of the heterologous FATP can result in loss of viability. A simple measure of viability is turbidity of the yeast suspension culture, which can be adapted to a high throughput screening assay for effects of various agents to be tested, using microtiter plates or similar devices for small-volume cultures  
10 of the engineered yeast cells.

Cell-free assays can also be used to measure the transport of fatty acids across a membrane, and therefor also to assess a test treatment or test agent for its effect on the rate or extent of fatty acid transport. An isolated FATP, for example in the presence of a detergent that preserves the native 3-dimensional structure of the FATP, or partially  
15 purified FATP, can be used in an artificial membrane system typically used to preserve the native conformation and activity of membrane proteins. Such systems include liposomes, artificial bilayers of phospholipids, isolated plasma membrane such as cell membrane fragments, cell membrane fractions, or cell membrane vesicles, and other systems in which the FATP can be properly oriented within the membrane to have  
20 transport activity. Assays for transport activity can be performed using methods analogous to those that can be used in cells engineered to predominantly express one FATP whose function is to be measured. A labeled (e.g., radioactively labeled) fatty acid substrate can be incubated with one side of a bilayer or in a suspension of liposomes constructed to integrate a properly oriented FATP. The accumulation of fatty  
25 acids with time can be measured, using appropriate means to detect the label (e.g., scintillation counting of medium on each side of the bilayer, or of the contents of liposomes isolated from the surrounding medium). Assays such as these can be adapted to use for the testing of agents which might interact with the FATP to produce an

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inhibitory or an enhancing effect on the rate or extent of fatty acid transport. That is, the above-described assay can be done in the presence or absence of the agent to be tested, and the results compared.

For examples of isolation of membrane proteins (ADP/ATP carrier and uncoupling protein), reconstitution into phospholipid vesicles, and assays of transport, see Klingenberg, M. *et al.*, *Methods Enzymol.* 260:369-389 (1995). For an example of a membrane protein (phosphate carrier of *Saccharomyces cerevisiae*) that was purified and solubilized from *E. coli* inclusion bodies, see Schroer, A. *et al.*, *J. Biol. Chem.* 273: 14269-14276 (1998). The Glut1 glucose transporter of rat has been expressed in yeast.

10 A crude membrane fraction of the yeast was prepared and reconstituted with soybean phospholipids into liposomes. Glucose transport activity could be measured in the liposomes (Kasahara, T. and Kasahara, M., *J. Biol. Chem.* 273: 29113-29117 (1998)). Similar methods can be applied to the proteins and polypeptides of the invention.

Another embodiment of the invention is a method for inhibiting fatty acid uptake in a mammal (e.g., a human), comprising administering to the mammal a therapeutically effective amount of an inhibitor of the transport function of one or more of the fatty acid transport proteins, thereby decreasing fatty acid uptake by cells comprising the fatty acid protein(s). Where it is desirable to reduce the uptake of fatty acids, for example, in the treatment of chronic obesity or as a part of a program of

20 weight control or hyperlipidemia control in a human, one or more inhibitors of one or more of the fatty acid transport proteins can be administered in an effective dose, and by an effective route, for example, orally, or by an indwelling device that can deliver doses to the small intestine. The inhibitor can be one identified by methods described herein, or can be one that is, for instance, structurally related to an inhibitor identified by

25 methods described herein (e.g., having chemical adducts to better stabilize or solubilize the inhibitor). The invention further relates to compositions comprising inhibitors of fatty acid uptake in a mammal, which may further comprise pharmaceutical carriers

suitable for administration to a subject mammal, such as sterile solubilizing or emulsifying agents.

A further embodiment of the present invention is a method of enhancing or increasing fatty acid uptake, such as enhancing or increasing LCFA uptake in the small intestine (e.g., to treat or prevent a malabsorption syndrome or other wasting condition) or in the liver (e.g., by an enhancer of FATP5 transport activity to treat acute liver failure) or in the kidney (e.g., by an enhancer of FATP2 transport activity to treat kidney failure). In this embodiment, a therapeutically effective amount of an enhancer of the transport function of one or more of the fatty acid transport proteins can be administered to a mammalian subject, with the result that fatty acid uptake in the small intestine is enhanced. In this embodiment, one or more enhancers of one or more of fatty acid transport proteins is administered in an effective dose and by a route (e.g., orally or by a device, such as an indwelling catheter or other device) which can deliver doses to the gut. The enhancer of FATP function (e.g., an enhancer of FATP4 function) can be identified by methods described herein or can be one that is structurally similar to an enhancer identified by methods described herein.

Aerobic reperfusion of ischemic myocardium is a common clinical event which can occur during such treatments as cardiac surgery, angioplasty, and thrombolytic therapy after a myocardial infarction. During reperfusion, a rapid recovery of myocardial energy production is essential for the complete recovery of contractile function. Not only the extent of recovery of myocardial energy metabolism but also the type of energy substrate used by the heart during reperfusion are important determinants of functional recovery. Circulating fatty acid levels increase following acute myocardial infarction or during cardiac surgery, such that during and following ischemia the heart muscle can be exposed to very high concentrations of fatty acids (Lopaschuk, G.D. and W. C. Stanley, *Science and Medicine* (November/December 1997)). High plasma fatty acid concentrations increase the severity of ischemic damage in a number of experimental models of cardiac ischemia and have been linked to

depression of mechanical function during aerobic reperfusion of previously ischemic hearts. Further data show that modifying fatty acid utilization can be beneficial for heart function in ischemia and can be a useful approach for the treatment of angina. See, e.g., Desideri and Celegon, *Am. J. Cardiol.* 82(5A):50K-53K; Lopaschuk, *Am. J. Cardiol.* 82(5A):14K-17K. Plasma fatty acid concentrations can be reduced by  
5 administering to a human subject or other mammal an effective amount of an inhibitor of a FATP such as FATP2 or FATP4, thereby providing a way of reducing fatty acid utilization by the heart.

In a further embodiment of the invention, a therapeutically effective amount of  
10 an inhibitor of hsFATP6 can be administered to a human patient by a suitable route, to reduce the uptake of fatty acids by cardiac muscle. This treatment is desirable in patients who are diagnosed as having, or who are at risk of, abnormal accumulations of fatty acids in the heart or a detrimentally high rate of uptake of fatty acids into the heart, because of ischemic heart disease, or following ischemia or trauma to the heart.

15 The invention further relates to antibodies that bind to an isolated or recombinant fatty acid transport protein of the FATP family, including portions of antibodies, which can specifically recognize and bind to one or more FATPs. The antibodies and portions thereof of the invention include those which bind to one or more FATPs of mouse or other mammalian species. In a preferred embodiment, the  
20 antibodies specifically bind to a naturally occurring FATP of humans. The antibodies can be used in methods to detect or to purify a protein of the present invention or a portion thereof by various methods of immunoaffinity chromatography, to inhibit the function of a protein in a method of therapy, or to selectively inactivate an active site, or to study other aspects of the structure of these proteins, for example.

25 The antibodies of the present invention can be polyclonal or monoclonal. The term antibody is intended to encompass both polyclonal and monoclonal antibodies. Antibodies of the present invention can be raised against an appropriate immunogen, including proteins or polypeptides of the present invention, such as an isolated or

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recombinant FATP1, FATP2, FATP3, FATP4, FATP5, FATP6, mtFATP, ceFATPa, ceFATPb, scFATP or portions thereof, or synthetic molecules, such as synthetic peptides (e.g., conjugated to a suitable carrier). Preferred embodiments are antibodies that bind to any of the following: hsFATP1, hsFATP2, hsFATP3, hsFATP4, hsFATP5  
5 or hsFATP6. The immunogen can be a polypeptide comprising a portion of a FATP and having at least one function of a fatty acid transport protein, as described herein.

The term antibody is also intended to encompass single chain antibodies, chimeric, humanized or primatized (CDR-grafted) antibodies and the like, as well as chimeric or CDR-grafted single chain antibodies, comprising portions from more than  
10 one species. For example, the chimeric antibodies can comprise portions of proteins derived from two different species, joined together chemically by conventional techniques or prepared as a single contiguous protein using genetic engineering techniques (e.g., DNA encoding the protein portions of the chimeric antibody can be expressed to produce a contiguous protein chain. See, e.g., Cabilly et al., U.S. Patent  
15 No. 4,816,567; Cabilly *et al.*, European Patent No. 0,125,023 B1; Boss *et al.*, U.S. Patent No. 4,816,397; Boss *et al.*, European Patent No. 0,120,694 B1; Neuberger, M.S. *et al.*, WO 86/01533; Neuberger, M.S. *et al.*, European Patent No. 0,194,276 B1; Winter, U.S. Patent No. 5,225,539; Winter, European Patent No. 0,239,400 B1; Queen  
20 *et al.*, U.S. Patent No. 5,585,089; and Queen *et al.*, European Patent No. EP 0 451 216 B1. See also, Newman, R. *et al.*, *BioTechnology*, 10:1455-1460 (1992), regarding primatized antibody, and Ladner *et al.*, U.S. Patent No. 4,946,778 and Bird, R.E. *et al.*, *Science*, 242:423-426 (1988) regarding single chain antibodies.)

Whole antibodies and biologically functional fragments thereof are also encompassed by the term antibody. Biologically functional antibody fragments which  
25 can be used include those fragments sufficient for binding of the antibody fragment to a FATP to occur, such as Fv, Fab, Fab' and F(ab')<sub>2</sub> fragments. Such fragments can be produced by enzymatic cleavage or by recombinant techniques. For instance, papain or pepsin cleavage can generate Fab or F(ab')<sub>2</sub> fragments, respectively. Antibodies can

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also be produced in a variety of truncated forms using antibody genes in which one or more stop codons have been introduced upstream of the natural stop site. For example, a chimeric gene encoding a F(ab')<sub>2</sub> heavy chain portion can be designed to include DNA sequences encoding the CH<sub>1</sub> domain and hinge region of the heavy chain.

5           Preparation of immunizing antigen (whole cells comprising FATP on the cell surface or purified FATP), and polyclonal and monoclonal antibody production can be performed using any suitable technique. A variety of methods have been described (See e.g., Kohler *et al.*, *Nature*, 256: 495-497 (1975) and *Eur. J. Immunol.* 6: 511-519 (1976); Milstein *et al.*, *Nature* 266: 550-552 (1977); Koprowski *et al.*, U.S. Patent No. 10 4,172,124; Harlow, E. and D. Lane, 1988, *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory: Cold Spring Harbor, NY); Chapter 11 In *Current Protocols In Molecular Biology*, Vol. 2 (containing supplements up through Supplement 42, 1998), Ausubel, F.M. *et al.*, eds., (John Wiley & Sons: New York, NY)). Generally, a hybridoma can be produced by fusing a suitable immortal cell line (e.g., a myeloma cell 15 line such as SP2/0) with antibody producing cells. The antibody producing cells, preferably those obtained from the spleen or lymph nodes, can be obtained from animals immunized with the antigen of interest. Immunization of animals can be by introduction of whole cells comprising fatty acid transport protein on the cell surface. The fused cells (hybridomas) can be isolated using selective culture conditions, and 20 cloned by limiting dilution. Cells which produce antibodies with the desired specificity can be selected by a suitable assay (e.g., ELISA).

Other suitable methods of producing or isolating antibodies (including human antibodies) of the requisite specificity can be used, including, for example, methods which select recombinant antibody from a library (e.g., Hoogenboom *et al.*, WO 93/06213; 25 Hoogenboom *et al.*, U.S. Patent No. 5,565,332; WO 94/13804, published June 23, 1994; and Dower, W.J. *et al.*, U.S. Patent No. 5,427,908), or which rely upon immunization of transgenic animals (e.g., mice) capable of producing a full repertoire of human antibodies (see e.g., Jakobovits *et al.*, *Proc. Natl. Acad. Sci. USA*, 90: 2551-2555



(1993); Jakobovits *et al.*, *Nature*, 362:255-258 (1993); Lonberg *et al.*, U.S. Patent No. 5,569,825; Lonberg *et al.*, U.S. Patent No. 5,545,806; Surani *et al.*, U.S. Patent No. 5,545,807; and Kucherlapati, R. *et al.*, European Patent No. EP 0 463 151 B1).

Another aspect of the invention is a method for directing an agent to cardiac muscle. The differential expression of FATP6 in cardiac muscle but not in other tissue types allows for the specific targeting of drugs, diagnostic agents, tagging labels, histological stains or other substances specifically to cardiac muscle. A targeting vehicle can be used for the delivery of such a substance. Targeting vehicles which bind specifically to FATP6 can be linked to a substance to be delivered to the cells of cardiac muscle. The linkage can be, for instance, via one or more covalent bonds, or by high affinity non-covalent bonds. A targeting vehicle can be an antibody, for instance, or other compound (e.g., a fatty acid or fatty acid analog) which binds to FATP6 with high specificity.

Targeting vehicles specific to the heart-specific protein FATP6 have *in vivo* (e.g., therapeutic and diagnostic) applications. For example, an antibody which specifically binds to FATP6 can be conjugated to a drug to be targeted to the heart (e.g., a cardiac glycoside to treat congestive heart failure, or  $\beta$ -adrenergic agents, sodium channel blockers or calcium channel blockers to treat arrhythmias). A substance (e.g., a radioactive substance) which can be detected (e.g., a label) *in vivo* can also be linked to a targeting vehicle which specifically binds to a heart-specific protein such as FATP6, and the conjugate can be used as a labeling agent to identify cardiac muscle cells.

Targeting vehicles specific to FATP6 find further applications *in vitro*. For example, an FATP6-specific targeting vehicle, such as an antibody (a polyclonal preparation or monoclonal) which specifically binds to FATP6, can be linked to a substance which can be used as a stain for a tissue sample (e.g., horseradish peroxidase) to provide a method for the identification of cardiac muscle in a sample, as can be used in embryology studies, for example.

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In a similar manner, an agent can be directed to the liver of a mammal, as FATP5 is expressed in liver but not in other tissue types. A targeting vehicle which specifically binds to FATP5 can be conjugated to a drug for delivery of the drug to the liver, such as a drug to treat hepatitis, Wilson's disease, lipid storage diseases and liver cancer. As with targeting vehicles specific to FATP6, targeting vehicles specific to FATP5 can be used in studying tissue samples *in vitro*.

The invention also relates to compositions comprising a modulator of FATP function. The term "modulate" as used herein refers to the ability of a molecule to alter the function of another molecule. Thus, modulate could mean, for example, inhibit, antagonize, agonize, upregulate, downregulate, induce, or suppress. A modulator has the capability of altering function of its target. Such alteration can be accomplished at any stage of the transcription, translation, expression or function of the protein, so that, for example, modulation of a target gene can be accomplished by modulation of the DNA or RNA encoding the protein, and the protein itself.

Antagonists or agonists (inhibitors or enhancers) of the FATPs of the invention, antibodies that bind a FATP, or mimetics of a FATP can be employed in combination with a non-sterile or sterile carrier or carriers for use with cells, tissues or organisms, such as a pharmaceutical carrier suitable for administration to a mammalian subject. Such compositions comprise, for instance, a media additive or a therapeutically effective amount of an inhibitor or enhancer compound to be identified by an assay of the invention and a pharmaceutically acceptable carrier or excipient. Such carriers may include, but are not limited to, saline, buffered saline, dextrose, water, ethanol, surfactants, such as glycerol, excipients such as lactose and combinations thereof. The formulation can be chosen by one of ordinary skill in the art to suit the mode of administration. The chosen route of administration will be influenced by the predominant tissue or organ location of the FATP whose function is to be inhibited or enhanced. For example, for affecting the function of FATP4, a preferred administration can be oral or through a tube inserted into the stomach (e.g., direct stomach tube or

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nasopharyngeal tube), or through other means to accomplish delivery to the small intestine. The invention further relates to diagnostic and pharmaceutical packs and kits comprising one or more containers filled with one or more of the ingredients of the aforementioned compositions of the invention.

5           Compounds of the invention which are FATPs, FATP fusion proteins, FATP mimetics, FATP gene-specific antisense poly- or oligonucleotides, inhibitors or enhancers of a FATP may be employed alone or in conjunction with other compounds, such as therapeutic compounds. The pharmaceutical compositions may be administered in any effective, convenient manner, including administration by topical, oral, anal,  
10   vaginal, intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, transdermal or intradermal routes, among others. In therapy or as a prophylactic, the active agent may be administered to an individual as an injectable composition, for example as a sterile aqueous dispersion, preferably isotonic.

          Alternatively, the composition may be formulated for topical application, for  
15   example, in the form of ointments, creams, lotions, eye ointments, eye drops, ear drops, mouthwash, impregnated dressings and sutures and aerosols, and may contain appropriate conventional additives, including, for example, preservatives, solvents to assist drug penetration, and emollients in ointments and creams. Such topical formulations may also contain compatible conventional carriers, for example cream or  
20   ointment bases, and ethanol or oleyl alcohol for lotions.

          In addition, the amount of the compound will vary depending on the size, age, body weight, general health, sex, and diet of the host, and the time of administration, the biological half-life of the compound, and the particular characteristics and symptoms of the disorder to be treated. Adjustment and manipulation of established dose ranges are  
25   well within the ability of those of skill in the art.

          A further aspect of the invention is a method to identify a polymorphism, or the presence of an alternative or variant allele of a gene in the genome of an organism (of interest here, genes encoding FATPs). As used herein, polymorphism refers to the

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occurrence of two or more genetically determined alternative sequences or alleles in a population. A polymorphic locus may be as small as a base pair. Polymorphic markers include restriction fragment length polymorphisms, variable number of tandem repeats (VNTR's), hypervariable regions, minisatellites, dinucleotide repeats, trinucleotide  
5 repeats, tetranucleotide repeats, simple sequence repeats, and insertion elements such as Alu. The first identified allelic form, or the most frequently occurring form can be arbitrarily designated as the reference (usually, "wildtype") form, and other allelic forms are designated as alternative (sometimes, "mutant" or "variant"). Diploid organisms may be homozygous or heterozygous for allelic forms.

10 An "allele" or "allelic sequence" is an alternative form of a gene which may result from at least one mutation in the nucleotide sequence. Alleles may result in altered mRNAs or polypeptides whose structure or function may or may not be altered. Any given gene may have none, one, or many allelic forms (polymorphism). Common mutational changes which give rise to alleles are generally ascribed to natural deletions,  
15 additions, or substitutions of nucleotides. Each of these types of changes may occur alone, or in combination with the others, one or more times in a given sequence.

Several different types of polymorphisms have been reported. A restriction fragment length polymorphism (RFLP) is a variation in DNA sequence that alters the length of a restriction fragment (Botstein *et al.*, *Am. J. Hum. Genet.* 32:314-331 (1980)).  
20 The restriction fragment length polymorphism may create or delete a restriction site, thus changing the length of the restriction fragment. RFLPs have been widely used in human and animal genetic analyses (see WO 90/13668; WO 90/11369; Donis-Keller, *Cell* 51:319-337 (1987); Lander *et al.*, *Genetics* 121:85-99 (1989)). When a heritable trait can be linked to a particular RFLP, the presence of the RFLP in an individual can  
25 be used to predict the likelihood that the individual will also exhibit the trait.

Other polymorphisms take the form of short tandem repeats (STRs) that include tandem di-, tri- and tetra-nucleotide repeated motifs. These tandem repeats are also referred to as variable number tandem repeat (VNTR) polymorphisms. VNTRs have

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been used in identity and paternity analysis (US 5,075,217; Armour *et al.*, *FEBS Lett.* 307:113-115 (1992); Horn *et al.*, WO 91/14003; Jeffreys, EP 370,719), and in a large number of genetic mapping studies.

Other polymorphisms take the form of single nucleotide variations between  
5 individuals of the same species. Such polymorphisms are far more frequent than  
RFLPs, STRs (short tandem repeats) and VNTRs (variable number tandem repeats).  
Some single nucleotide polymorphisms occur in protein-coding sequences, in which  
case, one of the polymorphic forms may give rise to the expression of a defective or  
other variant protein and, potentially, a genetic disease. Other single nucleotide  
10 polymorphisms occur in noncoding regions. Some of these polymorphisms may also  
result in defective protein expression (e.g., as a result of defective splicing). Other  
single nucleotide polymorphisms have no phenotypic effects.

Many of the methods described below require amplification of DNA from target  
samples and purification of the amplified products. This can be accomplished by PCR,  
15 for instance. See generally, *PCR Technology, Principles and Applications for DNA  
Amplification* (ed. H.A. Erlich), Freeman Press, New York, NY, 1992; *PCR Protocols:  
A Guide to Methods and Applications* (eds. Innis, et al.), Academic Press, San Diego,  
CA, 1990; Mattila *et al.*, *Nucleic Acids Res.* 19:4967 (1991); Eckert *et al.*, *PCR  
Methods and Applications* 1:17 (1991); *PCR* (eds. McPherson *et al.*, IRS Press,  
20 Oxford); and US 4,683,202.

Other suitable amplification methods include the ligase chain reaction (LCR)  
(see Wu and Wallace, *Genomics* 4:560 (1989); Landegren *et al.*, *Science* 241:1077  
(1988)), transcription amplification (Kwoh *et al.*, *Proc. Natl. Acad. Sci. USA* 86:1173  
(1989); self-sustained sequence replication (Guatelli *et al.*, *Proc. Natl. Acad. Sci. USA*  
25 87:1874 (1990), and nucleic acid based sequence amplification (NASBA). The latter  
two amplification methods involve isothermal reactions based on isothermal  
transcription, which produce both single stranded RNA (ssRNA) and double stranded

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DNA (dsDNA) as the amplification products in a ratio of about 30 or 100 to 1, respectively.

Another aspect of the invention is a method for detecting a variant allele of a human FATP gene, comprising preparing amplified, purified FATP DNA from a reference human and amplified, purified, FATP DNA from a "test" human to be compared to the reference as having a variant allele, using the same or comparable amplification procedures, and determining whether the reference DNA and test DNA differ in DNA sequence in the FATP gene, whether in a coding or a noncoding region, wherein, if the test DNA differs in sequence from the reference DNA, the test DNA comprises a variant allele of a human FATP gene. The following is a discussion of some of the methods by which it can be determined whether the reference FATP DNA and test FATP DNA differ in sequence.

Direct Sequencing. The direct analysis of the sequence of variant alleles of the present invention can be accomplished using either the dideoxy chain termination method or the Maxam and Gilbert method (see Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Press, New York 1989; Zyskind *et al.*, *Recombinant DNA Laboratory Manual*, Acad. Press, 1988)).

Denaturing Gradient Gel Electrophoresis. Amplification products generated using the polymerase chain reaction can be analyzed by the use of denaturing gradient gel electrophoresis. Different alleles can be identified based on the different sequence-dependent strand dissociation properties and electrophoretic migration of DNA in solution (chapter 7 in Erlich, ed. *PCR Technology, Principles and Applications for DNA Amplification*, W.H. Freeman and Co., New York, 1992).

Single-strand Conformation Polymorphism Analysis. Alleles of target sequences can be differentiated using single-strand conformation polymorphism analysis, which identifies base differences by alteration in electrophoretic migration of single stranded PCR products, as described in Orita *et al.*, *Proc. Natl. Acad. Sci. USA* 86:2766-2770 (1989). Amplified PCR products can be generated as described above,

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and heated or otherwise denatured, to form single-stranded amplification products. Single-stranded nucleic acids may refold or form secondary structures which are partially dependent on the base sequence. The different electrophoretic mobilities of single-stranded amplification products can be related to base-sequence differences  
5 between alleles of target sequences.

Detection of Binding by Protein That Binds to Mismatches. Amplified DNA comprising the FATP gene or portion of the gene of interest from genomic DNA, for example, of a normal individual is prepared, using primers designed on the basis of the DNA sequences provided herein. Amplified DNA is also prepared, in a similar manner,  
10 from genomic DNA of an individual to be tested for bearing a distinguishable allele. The primers used in PCR carry different labels, for example, primer 1 with biotin, and primer 2 with <sup>32</sup>P. Unused primers are separated from the PCR products, and the products are quantitated. The heteroduplexes are used in a mismatch detection assay using immobilized mismatch binding protein (MutS) bound to nitrocellulose. The  
15 presence of biotin-labeled DNA wherein mismatched regions are bound to the nitrocellulose via MutS protein, is detected by visualizing the binding of streptavidin to biotin. See WO 95/12689. MutS protein has also been used in the detection of point mutations in a gel-mobility-shift assay (Lishanski, A. *et al.*, *Proc. Natl. Acad. Sci. USA* 91:2674-2678 (1994)).

20 Other methods, such as those described below, can be used to distinguish a FATP allele from a reference allele, once a particular allele has been characterized as to DNA sequence.

Allele-specific probes. The design and use of allele-specific probes for analyzing polymorphisms is described by e.g., Saiki *et al.*, *Nature* 324:163-166 (1986);  
25 Dattagupta, EP 235,726, Saiki, WO 89/11548. Allele-specific probes can be designed so that they hybridize to a segment of a target DNA from one individual but do not hybridize to the corresponding segment from another individual due to the presence of different polymorphic forms in the respective segments from the two individuals.

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Hybridization conditions should be sufficiently stringent that there is a significant difference in hybridization intensity between alleles, and preferably an essentially binary response, whereby a probe hybridizes to only one of the alleles. Some probes are designed to hybridize to a segment of target DNA such that the polymorphic site aligns  
5 with a central position (e.g., in a 15-mer at the 7 position; in a 16-mer, at either the 8 or 9 position) of the probe. This design of probe achieves good discrimination in hybridization between different allelic forms.

Allele-specific probes are often used in pairs, one member of a pair showing a perfect match to a reference form of a target sequence and the other member showing a  
10 perfect match to a variant form. Several pairs of probes can then be immobilized on the same support for simultaneous analysis of multiple polymorphisms within the same target sequence.

Allele-specific Primers. An allele-specific primer hybridizes to a site on target DNA overlapping a polymorphism, and only primes amplification of an allelic form to  
15 which the primer exhibits perfect complementarity. See Gibbs, *Nucleic Acid Res.* 17:2427-2448 (1989). This primer is used in conjunction with a second primer which hybridizes at a distal site. Amplification proceeds from the two primers, resulting in a detectable product which indicates the particular allelic form is present. A control is usually performed with a second pair of primers, one of which shows a single base  
20 mismatch at the polymorphic site and the other of which exhibits perfect complementarity to a distal site. The single-base mismatch prevents amplification and no detectable product is formed. The method works best when the mismatch is included in the 3'-most position of the oligonucleotide aligned with the polymorphism because this position is most destabilizing to elongation from the primer (see, e.g., WO  
25 93/22456).

Gene Chips. Allelic variants can also be identified by hybridization to nucleic acids immobilized on solid supports (gene chips), as described, for example, in WO 95/11995 and U.S. Patent No. 5,143,854, both of which are incorporated herein by



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reference. WO 95/11995 describes subarrays that are optimized for detection of a characterized variant allele. Such a subarray contains probes designed to be complementary to a second reference sequence, which is an allelic variant of the first reference sequence.

- 5           The present method is illustrated by the following examples, which are not intended to be limiting in any way.

## EXAMPLES

### Materials and Methods

- The following Materials and Methods were used in the work described in  
10   Examples 1-5.

- Sequence Alignment of FATP Clones. The DNA sequence for mouse FATP1 was obtained from the National Center for Biotechnology Information nonredundant database. cDNAs for mmFATP2, 3, 4, and 5 were obtained by screening mouse expression libraries (purchased from GIBCO/BRL) with probes derived from the cloned  
15   expressed sequence tags (ESTs) (Research Genetics, Huntsville, AL). Full-length clones were obtained for mmFATP2 and 5 and partial sequences for mmFATP3 and 4. The sequences described herein have been deposited in the GenBank database (Accession Nos. FATP2, AF072760; FATP3, AF072759; FATP4, AF072758; FATP5, AF072757).

- 20           Neither FATP2 nor FATP5 contains an in-frame stop codon upstream of the putative initiator methionine; initiator methionines were assigned by homology with that in mmFATP1 and by the presence of a signal sequence immediately after it. The *Mycobacterium tuberculosis*, *Caenorhabditis elegans*, and *Saccharomyces cerevisiae* sequences were present in the dbEST database as part of the sequencing projects for  
25   these organisms. Sequences were aligned utilizing a ClustalX algorithm and the resulting alignment exported to SeqVu. Homologous amino acid substitutions are

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boxed in Figure 1 and were determined using the Dayhoff 250 method with a 50% homology cutoff.

Cell Transfection and LCFA Uptake. COS cells were cotransfected using the DEAE-dextran method with the mammalian expression vector pCDNA 3.1 (Invitrogen) expressing the gene for CD2 (pCDNA-CD2) in combination with either a pCDNA 3.1 or pCMVSPORT2 (GIBCO/BRL) expression vector containing one of the murine or nematode *FATP* genes (*pCDNA-mmFATP1*, *pCDNA-FATP2*, *pCMVSPORT-FATP5*, *pCDNA-ceFATPb*). Two days after transfection, cells were assayed for CD2 expression with a phycoerythrin-coupled anti-CD2(PE-CD2) monoclonal antibody (PharMingen), and fatty acid uptake was assayed with a BODIPY-labeled fatty acid analogue (Molecular Probes). Briefly, cells were washed twice with PBS (phosphate buffered saline) and stained with PE-CD2 at 4°C for 30 min in PBS containing 10% fetal calf serum. They were then washed three times with PBS/fetal calf serum for 5 min followed by an incubation for 2 min at 37°C in fatty acid uptake solution, which contained 0.1 µM BODIPY-FA and 0.1% fatty acid-free BSA (bovine serum albumin) in PBS (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436). After 2 min, the cells were washed four times with ice-cold PBS/0.1% BSA. The cells were then removed from the plates with PBS containing 5 mM EDTA and resuspended in PBS containing 10% fetal calf serum and 10 mM EDTA. PE-CD2 and BODIPY-FA fluorescence were measured using a FACScan (Becton Dickinson). COS cells were gated on forward scatter (FSC) and side scatter (SS). Cells exhibiting more than 300 CD2 fluorescence units (dsim) representing 15% of all cells were deemed CD2 positive and their BODIPY-FA fluorescence was quantitated.

*E. coli*-Based LCFA Uptake Assay. The full-length coding region of mtFATP and a control protein, the mammalian transcription factor TFE3, were subcloned into the inducible, prokaryotic expression vector pET (Novagen). Expression was induced with 1 mM isopropyl β-D-thiogalactoside (IPTG) for 1 hour, or cells were left uninduced. Cells were washed in PBS/0.1% BSA and resuspended in 1 ml PBS/0.1% BSA

containing 0.1  $\mu$ M [ $^3$ H]palmitate (NEN) at 37°C. Uptake was stopped after the indicated incubation time by transferring the cells onto filter paper using a cell harvester (Brandel, Bethesda, MD). Filters were washed extensively with ice-cold PBS/0.1% BSA, and [ $^3$ H]palmitate was quantitated by scintillation counting.

5 Northern Blots. Northern blot analysis of murine FATP expression was done using poly(A) mRNA blots (Clontech). Probes of each of the FATPs were derived from the 3' untranslated regions of each gene and were <60% identical in sequence. Probes were labeled by random priming (Boehringer Mannheim) and hybridized at 65°C. Blots were extensively washed in 0.2% SSC/0.1% SDS at 65°C.

10 Generation of Phylogenetic Trees. Complete and partial sequences for *FATP* genes from human, rat, mouse, puffer fish, *Drosophila melanogaster*, *C. elegans*, *S. cerevisiae*, and *M. tuberculosis* were aligned using ClustalX. A homologous region of 48 amino acids (residues 472-519 in mmFATP1) from all of the genes was used to determine phylogenetic relationship within ClustalX. Based on these data a  
15 phylogenetic tree was generated using Tree View PPC (Figure 5).

Nomenclature. It is proposed that the *FATP* genes be given a species specific prefix (mm, *Mus musculus*; hs, *Homo sapiens*; mt, *M. tuberculosis*; dm, *D. melanogaster*; ce, *C. elegans*; sc, *S. cerevisiae*) and numbered such that mammalian homologues in different species share the same number but differ in their prefix. Since  
20 the two *C. elegans* genes cannot be paired with a specific human or mouse FATP, they have been designated *ceFATPa* and *ceFATPb*.

#### Example 1: Identification of Novel Mammalian FATPs

The National Center for Biotechnology Information EST database was screened, using the mouse FATP protein sequence (mmFATP1), to identify novel FATPs. This  
25 strategy led to the identification of more than 50 murine EST sequences which could be assembled into five distinct contiguous DNA sequences (contigs). One contig was identical to the previously cloned FATP, which has been renamed FATP1. Another,

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which has been renamed FATP2, is the murine homologue of a rat gene previously identified by others as a very long chain acyl-CoA synthase (Uchiyama, A., Aoyama, T., Kamijo, K., Uchida, Y., Kondo, N., Orii, T. & Hashimoto, T. (1996) *J. Biol. Chem.* 271:30360-30365). The other three contigs represented novel genes (*FATP3*, 4, and 5).

5 Full-length clones for *FATP2* and *FATP5* and nearly complete sequences for *FATP3* and 4 (Figure 1) were obtained by screening cDNA libraries made from mouse day 10.5 embryos and adult liver. Also identified were human homologues for each of the murine genes in the EST database. A sixth human gene was also identified; whether this gene is also present in the mouse will require additional studies. Map positions are  
10 given in Tables 2 and 3.

The genetic loci for all of the human genes, with the exception of *FATP5* which was already mapped as an unknown EST, were determined using the radiation hybrid panels. The map positions given below show the distance (in centiRays) from the closest framework marker. As a guideline, there are approximately 300kb/cR.

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Table 2. Mapping Data for Human Genes

	hsFATP1	Chromosome Chr19 places 13.35 cR from WI-6344 (lod>3.0)
5	hsFATP2	Chromosome Chr15 places 4.92 cR from D15S126 (lod>3.0)
	hsFATP3	Chromosome Chr1 places 13.24 cR from WI-2862 (lod>3.0)
	hsFATP4	Chromosome Chr9 places 7.80 cR from WI-9685 (lod>3.0)
10	hsFATP5	unknown EST previously mapped to near D19S418
	hsFATP6	Chromosome Chr5 places 1.41 cR from WI-4907 (lod>3.0)

The mouse map is an internal backcross panel consisting of 188 mouse backcross DNA's plus 4 controls (B6, Spretus, F1, Water). The backcross was constructed by crossing B6 by Spretus animals and then crossing those F1's back to B6. Mapping is accomplished by taking advantage of recombinational events during meiosis, and the use of PCR primers to detect the differences (by size or re-annealing events) at any given locus between the B6 and Spretus allele.

For the purposes of mapping, a novel set of primers (gene of interest) is used to amplify from all 188 DNA's and then typed as being a B6 ("B") or a Spretus ("S"). This string of B's and S's is entered into the Map Manager program, which does a best fit calculation by comparing the string of 188 typings from the gene of interest to all loci already extant in the panel, for all 20 chromosomes. The gene of interest is then assigned to a particular area on a particular chromosome according to a number of parameters, including the minimalization of double cross-overs, and the highest LOD

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scores. Indicated in Table 3 are distances to the closest markers on either side of the FATP locus.

Table 3. Mapping Data for Mouse Genes

5	mmFATP1	Chromosome 8 places 2.82 cM from D8Mit132 (lod 43.4) and 1.81 cM from D8Mit74 (lod 43.5)
	mmFATP2	Chromosome 2 places 1.29 cM from D2Mit258 (lod 47.9) and 1.75 cM from D2NDS3 (lod 44.9)
10	mmFATP3	Chromosome 3 places 2.54 cM from D3Mit22 (lod 29.5) and 19.62 cM from D3Mit42 (lod 13.6)
15	mmFATP4	Chromosome 2 places 13.78 cM from D2Mit1 (lod 22.9) and 3.85 cM from D2Mit65 (lod 41.9)
	mmFATP5	Chromosome 7 places 7.28 cM proximal of D7Mit21 (lod 28.3)

## Example 2: Assessment of Function

The ability of the newly identified mouse genes to function as fatty acid transporters was assessed using a fluorescence-activated cell sorting-based assay. COS cells were transiently cotransfected with expression vectors encoding the cell surface protein CD2 and either mmFATP1, mmFATP2, or mmFATP5, respectively. Two days after transfection, COS cells were stained with an antibody to CD2 and then incubated with a BODIPY-labeled fatty acid [BODIPY-FA, (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436)]. The cells were then washed extensively, lifted off the dish, and

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analyzed by fluorescence-activated cell sorting. As judged by the number of CD2-positive cells, the transfection efficiency was approximately 20-30%. Fatty acid uptake was quantitated in the transiently transfected COS cells by measuring the BODIPY-FA fluorescence of the CD2-positive cells. Expression of CD2 had no effect on fatty acid uptake as shown by the finding that COS cells expressing only the transfected CD2 cDNA (CD2-positive) had the same low level of BODIPY-FA uptake as did untransfected (CD2-negative) control cells (Figure 2A, control). In COS cells cotransfected with CD2 and mmFATP1, mmFATP2, or mmFATP5, uptake of BODIPY-FA by the transfected (CD2-positive) cells was increased between 15- to 90-fold over control (CD2 cDNA only) cells (Figures 2A-2D).

### Example 3: Expression Patterns of Murine FATPs

Expression patterns of members of the murine *FATP* gene family were characterized by Northern blot analysis; to avoid cross-hybridization, the probes used were from the 3' untranslated region of these genes, which are less than 60% identical in sequence. The expression pattern of FATP1 agrees with that previously found (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436). Here, expression was seen primarily in heart and kidney. FATP2 is expressed almost exclusively in liver and kidney, which corresponds to the reported tissue distribution of the rat homologue [very long chain acyl-CoA (VLACS)] as assessed by Western blotting (Uchiyama, A., Aoyama, T., Kamijo, K., Uchida, Y., Kondo, N., Orii, T. & Hashimoto, T. (1996) *J. Biol. Chem.* 271:30360-30365). FATP3 is present in lung, liver, and testis. FATP5 is expressed only in liver and cannot be detected in other tissues even when the blot is overexposed. The human homologue of FATP5 is also liver specific and is not expressed in a wide array of other tissues tested, including fetal liver.

#### Example 4: FATPs Are Evolutionarily Conserved

The EST database was searched, using sequences conserved among the five murine FATP genes, for *FATP* genes in other organisms. Two homologues were found in *C. elegans* and one in *M. tuberculosis*. One of the *C. elegans* genes was cloned from a cDNA library and expressed in COS cells, as described for the murine FATPs. Overexpression of the nematode FATP resulted in a 15-fold increase of BODIPY-FA uptake compared with control cells (Figure 3). The mycobacterial *FATP* gene was isolated from a phage library and assessed for its ability to facilitate fatty acid uptake. *E. coli* transformed with a prokaryotic, isopropyl  $\beta$ -D-thiogalactoside-inducible expression vector containing the mycobacterial *FATP* gene demonstrated a significant increase in the rate of [ $^3$ H]palmitate uptake after induction, compared with uninduced bacteria or *E. coli* transformed with a control protein (Figure 4). Novel *FATP* genes were also identified in *F. rubripes* (puffer fish) and *D. melanogaster*.

#### Example 5: Phylogenetic Tree of FATPs

Faergeman *et al.* (Faergeman, N.J., DiRusso, C.C., Elberger, A., Knudsen, J. & Black, P. N. (1997) *J. Biol. Chem.* 272:8531-8538) identified three regions of very strong conservation between the *scFATP* and *mmFATP1* genes. The sequences of the FATPs were compared over a 311-amino acid FATP "signature sequence" which includes these conserved regions corresponding to amino acids 246-557 in mmFATP1 (underlined in Figure 1). When compared with the National Center for Biotechnology Information nonredundant database, only one region of the "FATP signature sequence" shows significant homology to other proteins. This small stretch of amino acids (underlined in Fig. 1) is an AMP-binding motif found in a multitude of other proteins, such as acyl-CoA synthase, several CoA lipases, and gramicidin S synthetase component II (Schaffer, J.E. & Lodish, H.F. (1994) *Cell* 79:427-436). The relevance of this motif to fatty acid transport is unclear. Other highly conserved regions among the FATPs, including long stretches of amino acids >90% identical from mycobacteria to



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humans, are not found in any other class of proteins. A 48-amino acid segment of the FATP signature sequence was used to construct a phylogenetic tree (Figure 5). Each of the human and mouse genes form their own branch; hsFATP6, which as yet has no murine homologue, is most closely related to hsFATP3 and mmFATP3. As expected, 5 rnVLACS is closer in sequence to mmFATP2 than to hsFATP2. The *FATP* genes of invertebrates i.e., *C. elegans* and *D. melanogaster*, are most closely related to each other. Surprisingly, the mycobacterial gene is more closely related to the human and mouse *FATP5* genes than to the FATPs of any of the lower organisms. Whether this reflects coevolution of the mycobacterial and human genes awaits further study.

## 10 Materials and Methods

The following materials and methods were used in the work described in Examples 6-10.

### Isolation of full-length human FATP1 and 4

Full-length clones encoding human FATP1 and human FATP4 were identified 15 by searching databases for sequences similar to murine FATP1-5 coding regions using the BlastX algorithm (Altschul *et al.*, *J. Mol. Biol.* 215: 403-410, 1990).

A concatamer of nucleotide sequences comprising the coding sequences of mmFATP1 (Genbank Accession U15976), mmFATP2, mmFATP3 (SEQ ID NO:6), mmFATP4 (SEQ ID NO:8) and mmFATP5 (SEQ ID NO:10) was used to search the 20 Millennium database using the BLASTX algorithm. Sequences with a score >150 were evaluated for whether they represented known FATP coding sequences.

Human clones with similarity to the 5' end of murine FATP sequences were sequenced completely. Clones encoding full-length human FATP1 were obtained from a heart cDNA library constructed in the mammalian expression vector pMET7 25 (Tartaglia *et al.*, *Cell*, 83: 1263-1271, 1995). Clones encoding full-length human FATP4 were obtained from a spleen cDNA library constructed in the mammalian expression vector pMET7.

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### Isolation of full-length human FATP6

Several clones encoding human FATP6 were identified by searching public databases as described above. Five clones were analyzed further by restriction digestion and DNA sequencing. One of these clones (Genbank Accession # AA412064) appeared  
5 to be full-length and its entire insert was sequenced.

### DNA Sequence Analysis

Sequences were aligned with the DNASTar program using the Clustal method. Hydrophobicity plots were generated with DNA Strider using the Kyte Doolittle method.

### 10 In situ hybridization

Tissues were collected from 8 week old C57/B16 mice. Tissues were fresh frozen, cut on a cryostat at 10  $\mu$ m thickness and mounted on Superfrost Plus slides (VWR). Sections were air dried for 20 minutes and then incubated with ice cold 4% paraformaldehyde (PFA)/phosphate buffered saline (PBS) for 10 minutes. Slides were  
15 washed 2 times 5 minutes with PBS, incubated with 0.25% acetic anhydride/1 M triethanolamine for 10 minutes, washed with PBS for 5 minutes and dehydrated with 70%, 80%, 95% and 100% ethanol for 1 minute each. Sections were incubated with chloroform for 5 minutes. Hybridizations were performed with  $^{35}$ S-radiolabeled ( $5 \times 10^7$  cpm/ml) cRNA probes generated from the 3' untranslated regions of mouse FATPs by  
20 PCR followed by *in vitro* transcription in the presence of 50% formamide, 10% dextran sulfate, 1x Denhardt's solution, 600 mM NaCl, 10 mM DTT, 0.25% SDS and 10  $\mu$ g/ml tRNA for 18 hours at 55°C. After hybridization, slides were washed with 10 mM Tris-HCl pH 7.6, 500 mM NaCl, 1 mM EDTA (TNE) for 10 minutes, incubated in 40  $\mu$ g/ml RNase A in TNE at 37°C for 30 minutes, washed in TNE for 10 minutes,  
25 incubated once in 2x SSC at 60°C for 1 hour, once in 0.2x SSC at 60°C for 1 hour, once in 0.2x SSC at 65°C for 1 hour and dehydrated with 50%, 70%, 80%, 90% and

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100% ethanol. Localization of mRNA transcripts was detected by dipping slides in Kodak NBT-2 photoemulsion and exposing for 7 days at 4°C, followed by development with Kodak Dektol developer. Slides were counter stained with haematoxylin and eosin and photographed. Controls for the in situ hybridization experiments include the  
5 use of a sense probe which showed no signal above background in all cases.

#### Northern Blotting

Human mRNA blots were obtained from Invitrogen or Clontech. PCR fragments from the 3' untranslated regions of human FATPs were used as probes. Blots were probed with <sup>32</sup>P-labeled DNA probes using the Rapid-Hyb buffer (Amersham)  
10 according to the manufacturer's instructions.

Cell transfection and LCFA uptake. COS cells were cotransfected, using lipofectamine (GIBCO BRL) according to the manufacturer's instructions, with the mammalian expression vector pCDNA3.1 (Invitrogen) expressing the gene for CD2 in combination with a pMET7 expression vector (Tartaglia *et al.*, *Cell*, 83:1263-1271,  
15 1995) containing hsFATP1 (pMET7-hsFATP1) or hsFATP4 (pMET7-hsFATP4) or pMET7 alone. Two days after transfection, cells were assayed for CD2 expression with a phycoerythrin-coupled anti-CD2 (PE-CD2) monoclonal antibody (PharMingen), and fatty acid uptake was assayed with a BODIPY-labeled fatty acid analog (Molecular Probes) as described above.

#### 20 Example 6: Determination of Expression of mmFATPs

mmFATP4, and to lesser extent mmFATP2, are expressed at high levels in the brush border layer of the small intestine.

Cell transfection and LCFA uptake. COS cells were cotransfected, using lipofectamine (GIBCO BRL) according to the manufacturer's instructions, with the  
25 mammalian expression vector pCDNA3.1 (Invitrogen) expressing the gene for CD2 in combination with a pMET7 expression vector (Tartaglia *et al.*, *Cell*, 83:1263-1271,

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1995) containing hsFATP1 (pMET7-hsFATP1) or hsFATP4 (pMET7-hsFATP4) or pMET7 alone. Two days after transfection, cells were assayed for CD2 expression with a phycoerythrin-coupled anti-CD2 (PE-CD2) monoclonal antibody (PharMingen), and fatty acid uptake was assayed with a BODIPY-labeled fatty acid analog (Molecular  
5 Probes) as described above.

Absorption of dietary fat requires transport of free fatty acids across the apical membrane of epithelial cells in the small intestine. Previous studies suggested that this transport is protein-mediated; however, the transport protein had not yet been identified. In situ hybridization was performed on each of the three regions of the small intestine --  
10 duodenum, jejunum and ileum -- as well as the colon, using probes from the 3' untranslated regions of mmFATP1, mmFATP2, mmFATP3, mmFATP4 and mmFATP5, to determine whether any of the mouse FATPs are expressed in the small intestine. It was expected that a protein involved in fatty acid absorption would be expressed in the epithelial cells of the small intestine, but absent from the colon.

15 Expression of mmFATPs in the jejunum was identical to that in the ileum in all cases. High levels of mmFATP4 mRNA were present in the epithelial cells of the jejunum and ileum, and lower, but significant, amounts were detected in the epithelial cells of the duodenum. Significantly, FATP4 mRNA was absent from other cell types of the small intestine and no FATP4 mRNA could be detected in any of the cells of the  
20 colon. FATP2 mRNA was present in the epithelial cells of the duodenum at a level similar to that of FATP4, but was present at lower levels in the jejunum and ileum. No signals above background were detected for mmFATP1, mmFATP3 and mmFATP5 in any of the intestinal tissues. mmFATP3 and FATP5 were clearly detectable by in situ hybridization in adult liver and mmFATP1 could be detected in a variety of tissues on a  
25 whole embryo in situ, indicating that the FATP1, 3, and 5 probes were working.

mmFATP4 expression is predominant in the small intestine compared to the other organs of the mouse embryo. In the small intestine, FATP4 expression is limited to differentiated enterocytes, while no signal is detected in the connective tissue or the

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undifferentiated epithelial cells in the crypts. Differentiated enterocytes are known to be the cells that mediate the uptake of fatty acids. FATP4 is specifically and strongly expressed in the epithelial cells of adult murine duodenum and ileum but not colon. Other FATPs, such as FATP5, are not expressed in the small intestine. Thus, FATP4 is  
5 the major FATP in the mouse small intestine. Given its high level of expression, it is likely that FATP4, and to a lesser extent FATP2, play an important role in the absorption of fatty acids.

mmFATP2, and mmFATP5 are expressed in hepatocytes

Northern analysis of mmFATP2, mmFATP3, mmFATP4 and mmFATP5  
10 showed expression in the liver. To determine whether these proteins are present in hepatocytes or other cells types present in liver homogenates, in situ hybridizations were performed. mmFATP2, and mmFATP5 mRNA was clearly present in hepatocytes, and was not concentrated in other cell types such as endothelial cells or macrophages. No signal above background was detected for mmFATP1 in any of the  
15 cell types in the liver, consistent with the results of the Northern blotting.

#### Example 7: Isolation and Sequence Analysis of Full-length Human FATP1 and Full-length Human FATP4

To identify human cDNA clones encoding FATP family members, Millennium databases were searched for sequences similar to murine FATP1-5 coding regions. Two  
20 clones were analyzed in detail; inspection of the entire DNA sequence of these two clones showed that they encode the human orthologs of mmFATP1 and mm FATP4, respectively. These two clones were designated hsFATP1 and hsFATP4, and their DNA and predicted protein sequences are shown in Figures 44A-44C and 45, and 50A-50C and 51. hsFATP1 is predicted to encode a 646 amino acid, 71 kD protein with  
25 multiple membrane-spanning domains (Figure 28A). HsFATP4 is predicted to encode a 643 amino acid, 72 kD protein with multiple membrane spanning domains (See Figure

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29A). A comparison of the DNA sequences of mouse and human FATP1 and mouse and human FATP4 (Figures 30A-30B and 31A-31B) shows that the mouse and human orthologs are 85% (FATP1) and 87% (FATP4) identical to each other within the coding sequences given in these figures. At the amino acid level, hsFATP1 and hsFATP4 are  
 5 ~90% identical to their respective mouse orthologs within the coding region shown in these figures (Figures 32 and 33). The sequence identities between mouse and human FATP1 and FATP4 are considerably higher than the ones observed between different FATP family members within one species (~40%-60%) and are present in the N-terminal part of the protein, a region that is poorly conserved between different FATP  
 10 family members. This high degree of sequence conservation clearly demonstrates that the newly identified human FATPs are orthologs of mouse FATP1 and FATP4 rather than novel FATP family members.

Table 4 is an identity/similarity matrix comparing the amino acid sequences of FATP1 and 4 from human and mouse. This shows that the gene whose sequence is  
 15 shown in Figure 43A is indeed human FATP4, since it is 91% identical with the murine FATP4 but only 62% identical with the closest related human FATP, which is FATP1.

Table 4				
Identity/Similarity Matrix				
	hsFATP4	mmFATP4	hsFATP1	mmFATP1
hsFATP4	---	93.2	72.3	72.0
20 mmFATP4	91.0	---	71.2	71.1
hsFATP1	61.9	61.0	---	92.4
mmFATP1	60.7	59.6	89.5	---

#### Example 8: Isolation and Sequence Analysis of Full-length Human FATP6

A search of EST databases identified a set of overlapping human sequences that  
 25 were similar to FATPs, but did not have a clear mouse ortholog. One of these EST

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clones was found to encode a full-length cDNA. The entire insert of this clone was sequenced and designated hsFATP6. The DNA and predicted protein sequences of hsFATP6 are shown in Figures 54A-54C and 55. HsFATP6 is predicted to encode a 619 amino acid, 70 kD protein with multiple membrane-spanning domains (Figure 35A). A comparison of the amino acid sequences of hsFATP6 with other human FATPs shows about 37% identity to either hsFATP1 or hsFATP4 (Figure 36). This degree of sequence identity is similar to what is observed between different mouse FATPs. The phylogenetic analysis described above clearly demonstrates that hsFATP6 is a member of the FATP family, but not an ortholog of any of the mouse FATPs.

10 Comparisons were done with "ALIGN" (E. Myers and W. Miller, "Optimal Alignments in Linear Space," *CABIOS* 4:11-17 (1988) using standard settings.

#### Example 9: Tissue Distribution of Human FATPs

The tissue distribution of human FATPs was assessed by Northern blotting. Human FATP3 was expressed in a large variety of tissues. In contrast, human FATP5 was present at high levels in the liver, but was undetectable in all other tissues examined. Thus, both hsFATP3 and hsFATP5 recapitulate the expression pattern of their mouse orthologs (see above). HsFATP6 is a novel FATP with no mouse ortholog as yet. Northern blotting shows that hsFATP6 is expressed at high levels in the heart, but is undetectable in other tissues, including skeletal and smooth muscle. This tissue distribution suggests that human FATP6 performs an important role in energy metabolism in the heart; blocking FATP6-mediated fatty acid transport may therefore be beneficial for a number of heart diseases, e.g., ischemic heart disease.

15  
20

To identify the major FATP expressed in the human small intestine, Northern blotting was performed on a blot containing mRNA from human stomach, jejunum, ileum, colon, rectum and lung. hsFATP5 and hsFATP6 were undetectable in any of these tissues. FATP5 is only expressed in liver and FATP6 only in heart. hsFATP2 was weakly expressed in the colon, and an even weaker signal was detectable in

25

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jejunum, ileum and lung lanes. hsFATP3 was expressed well in the lung, but was only weakly expressed in the other tissues tested. Importantly, no difference was seen in the expression of hsFATP3 between small intestine and stomach or colon, suggesting that the expression observed is not related to fatty acid absorption in the small intestine.

- 5 hsFATP4 was clearly expressed in both jejunum and ileum; expression was significantly lower in the colon and was absent in the stomach. This expression pattern is consistent with a major role for FATP4 in absorption of fatty acids in the human gut.

#### Example 10: Expression of hsFATP1 and hsFATP4 Promotes Transport of Fatty Acids

- COS cells were cotransfected using lipofectamine with the mammalian  
10 expression vector pCDNA-CD2 in combination with one of the FATP-containing expression vectors (pMET7-hsFATP1 or pMET7-hsFATP4) or an insertless expression vector (pMET7, control) as described in Materials and Methods for Examples 6-10. COS cells were gated on forward scatter and side scatter. Cells exhibiting more than 400 CD2 fluorescence units representing ~30% of all cells were deemed CD2-positive.  
15 The percent of CD2-positive cells exhibiting a BODIPY-fluorescence of >300 is plotted for the three different vectors tested (Figure 37).

#### Example 11: Stable Expression of Human FATP4 in 293 Cells

- Stable cell lines were generated as follows. A DNA fragment containing the entire hsFATP4 coding sequence as well as 100 nucleotides of 5' and 50 nucleotides of  
20 3' untranslated region was inserted into the vector pIRES-neo (Clontech) using standard cloning techniques. The resulting construct or a vector control (pIRES-neo) was transfected into 293 cells using the lipofectamine method (Gibco BRL) according to the manufacturer's directions. Cells that had taken up the DNA were selected with 1 mg/ml G418 (Gibco BRL). Single colonies were picked 1 to 2 weeks after transfection and  
25 grown in medium containing 0.8 mg/ml G418. Colonies were screened for the ability to take up fatty acids by measuring uptake of a fluorescently labeled fatty acid (BODIPY-



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FA). About 40 colonies transfected with the pIRES-neo containing FATP4 and ~20 colonies transfected with pIRES-neo control were analyzed. All 20 of the vector control clones showed amounts of BODIFY-FA uptake similar to each other and to untransfected 293 cells. In contrast, among the 40 FATP4 transfected clones, 3 had a 5- to 10-fold increased BODIPY-FA uptake compared to any of the vector controls, and a large number (~20) showed an approximately two-fold increase in BODIPY-FA levels. This distribution is consistent with FATP4 conferring increased fatty acid uptake in these cells. One of the cell lines with the highest amount of BODIPY-FA uptake was selected to be used for measuring uptake of tritiated fatty acid.

10       The uptake of tritiated oleate over time by either FATP4 expressing or control cells was assayed over time. Expression of FATP4 increases the rate of fatty acid uptake by over 3-fold, demonstrating that FATP4 is, like the other FATPs, a functional fatty acid transporter (Figure 38).

#### Example 12: Immuno-staining with FATP4-Specific Antiserum

15       A polyclonal antiserum against the C-terminus of mmFATP4 was raised using a GST-fusion protein having mmFATP4-specific amino acid sequence 552-643 (AVASP...GEEKL). In western blot experiments, the purified antibody reacted strongly with a synthetic peptide matching the C-terminus of mmFATP4, but not with a corresponding region of mmFATP2, mmFATP3, or mmFATP5. The mmFATP4 specific polyclonal antiserum detects, in western blot experiments with enterocyte lysates from 3 different mice, a ~70 kDa protein, which is in accordance with mmFATP4's predicted molecular weight of 72 kDa. The binding is specific for mmFATP4, since it can be completely abolished by preincubation of the antiserum with the GST-fusion peptide used to raise the antibody.

25       Immunofluorescence experiments were performed using the anti-mmFATP4 antiserum on fresh frozen sections of murine small intestine. The antibody binding demonstrates strong expression of mmFATP4 in enterocytes, confirming the results of

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the in situ hybridization experiments. At higher magnifications it is apparent that mmFATP4 is expressed at the apical side of the enterocyte, indicating that the transporter is present in the brush border membrane, which is known to mediate the uptake of fatty acids from the intestinal lumen.

5           Immuno-electron microscopy studies were performed on fresh frozen murine intestinal cells. The gold particles used, appearing as black specks on the electron micrographs, indicate the subcellular localization of mmFATP4 to be on the microvilli of the enterocyte. It can be seen from the electron micrographs that mmFATP4 is localized exclusively in membranes, preferentially the apical plasma membrane,  
10       confirming that it is indeed a membrane protein.

#### Example 13: Inhibition of Fatty Acid Uptake Specific to FATP4 Demonstrated in Isolated Mouse Enterocytes

Phosphorothioate derivatives of the following oligonucleotides were synthesized:

15	FATP4-AS2	CCCCCACCAGAGAGGCTCC (SEQ ID NO:100)
	FATP4-AS2MM	CCACCCCCGGAAAGCCTGC (SEQ ID NO:101)
	FATP4-S2	GGAGCCTCTCTGGTGGGGG (SEQ ID NO:102)

FATP4 AS2 is the antisense oligo; it is designed to be complementary to the sequence extending from nucleotide 10 to nucleotide 28 of the mouse FATP4 coding sequence.  
20   FATP4-AS2MM is a control oligo; in the oligo every third nucleotide was changed creating mismatches; the overall nucleotide composition is identical to FATP4-AS2 (same number of G, A, T, C). FATP4-S2 is the sense control.

Enterocytes were isolated from the small intestine of mice and incubated for 48h in tissue culture (Figure 40) either without oligonucleotides (squares) or with 100  $\mu$ M  
25   FATP4 specific sense (circles) or antisense (diamonds) oligonucleotides. The uptake over time of 25  $\mu$ M oleate was then measured. While the FATP4 sense oligonucleotide

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did not significantly influence the uptake, the antisense oligonucleotide inhibited fatty acid uptake by ~50%.

The effect of either FATP4 sense, antisense or mismatch sequence oligonucleotides on the uptake of fatty acids was measured in enterocytes. Isolated enterocytes were incubated with increasing concentrations of FATP4 antisense oligonucleotides (solid bars in Figure 41), or a mismatch control oligonucleotide with identical nucleotide composition (stippled bars), or with 100  $\mu$ M of the FATP4 sense-oligonucleotide (lined bar). The medium for this incubation was Dulbecco's modified Eagle's medium with 4.5 g/L glucose, 1 mM sodium pyruvate, 0.01 mg/ml human transferrin and 10% fetal bovine serum. After 48 hours of incubation the uptake of oleate by enterocytes was measured over a 5 minute time interval. Measurements were done in quadruplicate. The uptake assay was done in Hank's buffered salt solution with 10 mM taurocholate. Only the enterocytes given FATP4 antisense oligonucleotide showed a concentration dependent decrease of fatty acid uptake, inhibiting it at a 100  $\mu$ M concentration by ~50%. This effect was FATP4 specific, since only the antisense oligonucleotide which can bind to the FATP4 mRNA and block its translation inhibited uptake, but not a control oligonucleotide differing only in the sequence but not the nucleotide content, ruling out a toxic or otherwise nonspecific inhibitory effect of this oligonucleotide due to its chemical composition.

As a further control experiment, the uptake of oleate was measured along with the uptake of methionine in the same cultured enterocytes. Antisense oligonucleotide, mismatch sequence oligonucleotide, or no oligonucleotide was added to a concentration of 100  $\mu$ M to cultures of enterocytes. After incubation for 48 hours, the uptake of both  $^3$ H-labeled oleate and  $^{35}$ S-labeled methionine was assayed. Results are shown in Figure 42. Fatty acid uptake is at the left side of the paired bars; methionine uptake is on the right side of the paired bars. The fact that amino acid uptake was not influenced by the antisense oligonucleotide treatment further supports the conclusion that the antisense oligonucleotide causes a specific reduction in translation of FATP4-specific mRNA.

Example 14: mmFATP2 Is Expressed in Proximal Renal Tubule Epithelium

Northern analysis showed that mmFATP1, mmFATP2, and mmFATP4 are present in the kidney. In situ hybridization (methods as for Example 6) was performed to determine which cell type(s) of the kidney these mRNAs are expressed in.

- 5 mmFATP1 mRNA was present in virtually all cells throughout the kidney with no obvious preference for a particular cell type. In contrast, mmFATP2 was expressed only in the renal cortex. Within the cortex, expression of mmFATP2 was restricted to the epithelial cells of the proximal renal tubules. The primary function of proximal renal tubule cells is the reabsorption of filtered salts and nutrients (e.g., glucose), a
- 10 process that requires mitochondrial oxidation and that can utilize fatty acids as energy substrates. Based on the localization of mmFATP2, it is possible that mmFATP2 is important for reabsorption in the kidney by allowing uptake of an energy source (fatty acids) from the blood into renal epithelial cells. Alternatively, if fatty acids need to be reabsorbed in the kidney, similarly to glucose, FATP2 could be involved in the
- 15 reabsorption of fatty acids. Determination of the subcellular localization of FATP2 will distinguish between these two possibilities.

Table 5 summarizes data on expression of the mouse FATPs in various organs.

Table 5. Mouse FATP mRNA Expression

Mouse Probes	mFATP1	mFATP2	mFATP3	mFATP4	mFATP5
E18.5 embryo expression	everywhere, brain = thymus> heart> brown fat, others	liver (hepatocytes)	-	Brain, small intestine, superior cervical ganglion (SCG), dorsal root ganglion (DRG), other regions have lower expression	Mouse Probes
Duodenum	-	villi (surface epithelium)	-	villi (surface epithelium)	-
Jejunum	-	villi (surface epithelium)	-	villi (surface epithelium)	-
Ileum	-	villi (surface epithelium)	-	villi (surface epithelium)	-
Colon	low expression in the crypt	very low level in the crypt	-	-	-
Kidney	cortex and medulla	proximal tubules	-	-	-

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Table 5 (continued). Mouse FATP mRNA Expression

Mouse Probes	mFATP1	mFATP2	mFATP3	mFATP4	mFATP5
Liver	-	hepatocytes	hepatocytes	-	hepatocytes
Pancreas	exocrine secretory units or acinar cells; endocrine pancreas (islet) are negative	exocrine secretory units or acinar cells; endocrine pancreas (islet) are negative	-	-	-
Brain	Neuronal expression throughout the brain including hypothalamus	-	-	Neuronal expression throughout the brain including hypothalamus	-
Heart	myocytes	-	-	-	-
Testis	seminiferous tubules	-	seminiferous tubules	-	-
Lung	bronchiole	-	-	-	-
Adipose	adipocyte	adipocyte	-	-	-

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## Example 15: Isolation of full-length human FATP3

Full-length clones encoding human FATP3 were identified by searching databases for sequences similar to the murine FATP1-5 coding regions using the BlastX algorithm (Altschul *et al.*, *J. Mol. Biol.* 215: 403-410, 1990). Human clones with  
5 similarity to the 5' end of murine FATP sequences were sequenced completely. A clone encoding full-length human FATP3 was obtained from a human bone library constructed in the mammalian expression vector pMET7 (Tartaglia, L.A. *et al.*, *Cell* 83: 1263-1271, 1995). To identify human cDNA clones encoding FATP family members, databases were searched for sequences similar to murine FATP1-5 coding regions. One  
10 clone was found to encode the human ortholog of mmFATP3 and was designated hsFATP3. The DNA and predicted protein sequences of hsFATP3 are shown in Figures 94A and 94B. hsFATP5 is predicted to encode a 703 amino acid 75.6 kD protein with multiple membrane-spanning domains. A comparison of the DNA sequences of mouse and human FATP3 shows that the mouse and human orthologs are 81% identical to  
15 each other within the coding region. At the amino acid level, hsFATP3 is ~86% identical to mm FATP3 within the coding region. The sequence identities between mouse and human FATP3 are considerably higher than those observed between different FATP family members within one species (~40%) and are present in the N-terminal part of the protein, a region that is poorly conserved between different FATP  
20 family members.

All references cited herein are incorporated by reference in their entirety.

While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the  
25 spirit and scope of the invention as defined by the appended claims.

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## CLAIMS

What is claimed is:

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
  - 5 a) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP2 in SEQ ID NO:49;
  - b) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP4 in SEQ ID NO:53; and
  - 10 c) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP6 in SEQ ID NO:57.
2. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
  - a) the nucleotide sequence in SEQ ID NO:48;
  - b) the nucleotide sequence in SEQ ID NO:52; and
  - 15 c) the nucleotide sequence in SEQ ID NO:56.
3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
  - a) a nucleotide sequence which is complementary to the nucleotide sequence of FATP2 in SEQ ID NO:48;
  - 20 b) a nucleotide sequence which is complementary to the nucleotide sequence of FATP4 in SEQ ID NO:52; and
  - c) a nucleotide sequence which is complementary to the nucleotide sequence of FATP6 in SEQ ID NO:56.



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4. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
  - a) a nucleotide sequence which consists of the coding region of FATP2;
  - b) a nucleotide sequence which consists of the coding region of FATP4;
  - 5 and
  - c) a nucleotide sequence which consists of the coding region of FATP6.
  
5. An isolated nucleic acid molecule comprising at least 15 contiguous nucleotides of a nucleotide sequence selected from the group consisting of :
  - a) SEQ ID NO:48, or of the complement thereof;
  - 10 b) SEQ ID NO:52, or of the complement thereof; and
  - c) SEQ ID NO:56, or of the complement thereof.
  
6. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a contiguous portion of at least about 15 amino acids of a sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ  
15 ID NO:56.
  
7. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a  
20 sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ ID NO:56.
  
8. An isolated nucleic acid molecule having at least 90% nucleotide sequence identity to a nucleic acid encoding a polypeptide comprising an amino acid

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sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.

9. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide, wherein said nucleotide sequence is at least 95% similar to the nucleotide sequence of a nucleotide sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ ID NO:56.
10. An isolated nucleic acid encoding a fatty acid transport protein having an amino acid sequence sharing at least about 95% amino acid sequence similarity with an amino acid sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.
11. An isolated nucleic acid molecule encoding a fusion polypeptide, said nucleic acid molecule comprising a nucleotide sequence encoding a portion of an amino acid sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57, and further comprising a nucleotide sequence encoding a heterologous portion of said fusion polypeptide.
12. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
  - a) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP2 in SEQ ID NO:49;
  - b) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP4 in SEQ ID NO:53; and
  - c) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP6 in SEQ ID NO:57.

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13. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- a) the nucleotide sequence of FATP2 in SEQ ID NO:48;
  - b) the nucleotide sequence of FATP4 in SEQ ID NO:52; and
  - 5 c) the nucleotide sequence of FATP6 in SEQ ID NO:56.
14. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which is complementary to the nucleotide sequence of FATP2 in SEQ ID NO:48;
  - 10 b) a nucleotide sequence which is complementary to the nucleotide sequence of FATP4 in SEQ ID NO:52; and
  - c) a nucleotide sequence which is complementary to the nucleotide sequence of FATP6 in SEQ ID NO:56.
15. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which consists of the coding region of FATP2;
  - b) a nucleotide sequence which consists of the coding region of FATP4; and
  - c) a nucleotide sequence which consists of the coding region of FATP6.
- 20 16. A host cell comprising the vector of Claim 15.
17. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a

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nucleic acid molecule consisting of a sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ ID NO: 56.

18. A vector comprising a nucleic acid comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a nucleic acid molecule consisting of a sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, and SEQ ID NO:56.
19. A host cell comprising the vector of Claim 8.
20. A method for producing a polypeptide which is a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, said method comprising culturing the host cell of Claim 19 under conditions in which the nucleic acid molecule is expressed, thereby producing the polypeptide.
21. A vector comprising a nucleic acid having at least 90% nucleotide sequence identity to a nucleic acid encoding a polypeptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.
22. A host cell comprising the vector of Claim 21.
23. A method for producing a polypeptide, said method comprising culturing the host cell of Claim 22 under conditions in which the nucleic acid molecule is expressed, thereby producing the polypeptide.

24. A vector comprising a nucleic acid encoding a fatty acid transport protein having an amino acid sequence sharing at least about 95% amino acid sequence similarity with an amino acid sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.
- 5 25. A host cell comprising the vector of Claim 24.
26. A method for producing a fatty acid transport protein, said method comprising culturing the host cell of Claim 25 under conditions in which the nucleic acid molecule is expressed, thereby producing the fatty acid transport protein.
- 10 27. A vector comprising a nucleic acid encoding a fusion polypeptide, said nucleic acid comprising a nucleotide sequence which encodes a contiguous portion of at least about 15 amino acids of a sequence selected from the group consisting of SEQ ID NO:49, SEQ ID NO:53, and SEQ ID NO:57.
28. A host cell comprising the vector of Claim 27.
- 15 29. A method for producing a fusion polypeptide, said method comprising culturing the host cell of Claim 28 under conditions in which the nucleic acid is expressed, thereby producing the fusion polypeptide.
30. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- 20 a) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP1 in SEQ ID NO:47;
- b) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP3 in SEQ ID NO:51; and

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- c) a nucleotide sequence which encodes a protein consisting of the amino acid sequence of FATP5 in SEQ ID NO:102.
31. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- 5 a) the nucleotide sequence in SEQ ID NO:46;  
b) the nucleotide sequence in SEQ ID NO:50; and  
c) the nucleotide sequence in SEQ ID NO:101.
32. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- 10 a) a nucleotide sequence which is complementary to the nucleotide sequence of FATP1 in SEQ ID NO:46;  
b) a nucleotide sequence which is complementary to the nucleotide sequence of FATP3 in SEQ ID NO:50; and  
c) a nucleotide sequence which is complementary to the nucleotide  
15 sequence of FATP5 in SEQ ID NO:101.
33. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which consists of the coding region of FATP1;  
b) a nucleotide sequence which consists of the coding region of FATP3;  
20 and  
c) a nucleotide sequence which consists of the coding region of FATP5.
34. An isolated nucleic acid molecule comprising at least 15 contiguous nucleotides of a nucleotide sequence selected from the group consisting of:
- a) SEQ ID NO:46, or of the complement thereof;

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- b) SEQ ID NO:50, or of the complement thereof; and
- c) SEQ ID NO:101, or of the complement thereof.

35. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a contiguous portion of at least about 15 amino acids of a sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102.
- 5
36. An isolated nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO:50, and SEQ ID NO:101.
- 10
37. An isolated nucleic acid molecule having at least 90% nucleotide sequence identity to a nucleic acid encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102.
- 15
38. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide, wherein said nucleotide sequence is at least 90% identical to the nucleotide sequence of a nucleotide sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO:50, and SEQ ID NO:101, and wherein said percent identity is calculated using the GAP program in the GCG software package, using a gap weight of 5.000 and a length weight of 0.100.
- 20

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39. An isolated nucleic acid encoding a fatty acid transport protein having an amino acid sequence sharing at least about 95% amino acid sequence similarity with an amino acid sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102.
- 5 40. An isolated nucleic acid molecule encoding a fusion polypeptide, said nucleic acid molecule comprising a nucleotide sequence encoding a portion of an amino acid sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102, and further comprising a nucleotide sequence encoding a heterologous portion of said fusion polypeptide.
- 10 41. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP1 in SEQ ID NO:47;
  - b) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP3 in SEQ ID NO:51; and
  - 15 c) a nucleotide sequence which encodes a protein comprising the amino acid sequence of FATP5 in SEQ ID NO:102.
42. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- 20 a) the nucleotide sequence of FATP1 in SEQ ID NO:46;
  - b) the nucleotide sequence of FATP3 in SEQ ID NO:50; and
  - c) the nucleotide sequence of FATP5 in SEQ ID NO:101.
43. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:



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- a) a nucleotide sequence which is complementary to the nucleotide sequence of FATP1 in SEQ ID NO:46;
- b) a nucleotide sequence which is complementary to the nucleotide sequence of FATP3 in SEQ ID NO:50; and
- 5 c) a nucleotide sequence which is complementary to the nucleotide sequence of FATP5 in SEQ ID NO:101.
44. A vector comprising a nucleic acid comprising a nucleotide sequence selected from the group consisting of:
- a) a nucleotide sequence which consists of the coding region of FATP1;
- 10 b) a nucleotide sequence which consists of the coding region of FATP3; and
- c) a nucleotide sequence which consists of the coding region of FATP5.
45. A host cell comprising the vector of Claim 44.
46. An isolated nucleic acid molecule comprising a nucleotide sequence which
- 15 encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a nucleic acid molecule consisting of a sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO:50, and SEQ ID NO:101.
- 20 47. A vector comprising a nucleic acid comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, wherein said nucleic acid molecule hybridizes under high stringency conditions to a complement of a

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nucleic acid molecule consisting of a sequence selected from the group consisting of SEQ ID NO:46, SEQ ID NO:50, and SEQ ID NO:101.

48. A host cell comprising the vector of Claim 47.
49. A method for producing a polypeptide which is a naturally occurring allelic  
5 variant of a polypeptide consisting of the amino acid sequence of a fatty acid transport protein, said method comprising culturing the host cell of Claim 48 under conditions in which the nucleic acid molecule is expressed, thereby producing the polypeptide.
50. A vector comprising a nucleic acid having at least 90% nucleotide sequence  
10 identity to a nucleic acid encoding a polypeptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102.
51. A host cell comprising the vector of Claim 50.
52. A method for producing a polypeptide, said method comprising culturing the  
15 host cell of Claim 51 under conditions in which the nucleic acid molecule is expressed, thereby producing the polypeptide.
53. A vector comprising a nucleic acid encoding a fatty acid transport protein having  
an amino acid sequence sharing at least about 95% amino acid sequence  
similarity with an amino acid sequence selected from the group consisting of  
20 SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102.
54. A host cell comprising the vector of Claim 53.

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55. A method for producing a fatty acid transport protein, said method comprising culturing the host cell of Claim 54 under conditions in which the nucleic acid molecule is expressed, thereby producing the fatty acid transport protein.
56. A vector comprising a nucleic acid encoding a fusion polypeptide, said nucleic acid comprising the nucleotide sequence which encodes a contiguous portion of at least about 15 amino acids of a sequence selected from the group consisting of SEQ ID NO:47, SEQ ID NO:51, and SEQ ID NO:102, said nucleic acid further comprising a nucleotide sequence encoding a heterologous portion of said fusion polypeptide.
57. A host cell comprising the vector of Claim 56.
58. A method for producing a fusion polypeptide, said method comprising culturing the host cell of Claim 57 under conditions in which the nucleic acid is expressed, thereby producing the fusion polypeptide.
59. Isolated FATP2 or a functional portion thereof.
60. An isolated polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO:49.
61. An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:49.
62. An isolated polypeptide comprising an amino acid sequence which is at least 97% identical to the amino acid sequence of SEQ ID NO:49.

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63. Isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said nucleic acid molecule hybridizes to a complement of a nucleic acid molecule consisting of SEQ ID NO:48 under high stringency conditions.
64. An isolated polypeptide comprising an amino acid sequence in SEQ ID NO:49.
65. A fusion protein comprising a polypeptide or peptide selected from the group consisting of:
- a) a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2 in SEQ ID NO:49;
  - b) a polypeptide consisting of an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:49;
  - c) a polypeptide consisting of an amino acid sequence in SEQ ID NO:49; and
  - d) a peptide comprising a contiguous portion of at least about 15 amino acid residues of any of the foregoing.
66. The fusion protein of Claim 65 wherein the fusion protein transports fatty acids across a cell membrane or an artificial cell membrane system.
67. The fusion protein of Claim 65, further comprising an affinity ligand.
68. Isolated FATP4 or a functional portion thereof.
69. An isolated polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO:53.

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70. An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:53.
71. An isolated polypeptide comprising an amino acid sequence which is at least 97% identical to the amino acid sequence of SEQ ID NO:53.
- 5 72. Isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said nucleic acid molecule hybridizes to a complement of a nucleic acid molecule consisting of SEQ ID NO:52 under high stringency conditions.
- 10 73. An isolated polypeptide comprising an amino acid sequence in SEQ ID NO:53.
74. A fusion protein comprising a polypeptide or peptide selected from the group consisting of:
- a) a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4 in SEQ ID NO:53;
- 15 b) a polypeptide consisting of an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:53;
- c) a polypeptide consisting of an amino acid sequence in SEQ ID NO:53; and
- d) a peptide comprising a contiguous portion of at least about 15 amino acid residues of any of the foregoing.
- 20 75. The fusion protein of Claim 74 wherein the fusion protein transports fatty acids across a cell membrane or an artificial cell membrane system.

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76. The fusion protein of Claim 74, further comprising an affinity ligand.
77. Isolated FATP6 or a functional portion thereof.
78. An isolated polypeptide comprising an amino acid sequence which is at least 90% identical to the amino acid sequence of SEQ ID NO:57.
- 5 79. An isolated polypeptide comprising an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:57.
80. An isolated polypeptide comprising an amino acid sequence which is at least 97% identical to the amino acid sequence of SEQ ID NO:57.
- 10 81. Isolated polypeptide encoded by a nucleic acid molecule comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said nucleic acid molecule hybridizes to a complement of a nucleic acid molecule consisting of SEQ ID NO:56 under high stringency conditions.
82. An isolated polypeptide comprising an amino acid sequence in SEQ ID NO:57.
- 15 83. A fusion protein comprising a polypeptide or peptide selected from the group consisting of:
- a) a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6 in SEQ ID NO:57;
  - b) a polypeptide consisting of an amino acid sequence which is at least 95% identical to the amino acid sequence of SEQ ID NO:57;
- 20

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- c) a polypeptide consisting of an amino acid sequence in SEQ ID NO:57;  
and
  - d) a peptide comprising a contiguous portion of at least about 15 amino acid  
residues of any of the foregoing.
- 5    84.    The fusion protein of Claim 83 wherein the fusion protein transports fatty acids  
across a cell membrane or an artificial cell membrane system.
85.    The fusion protein of Claim 83, further comprising an affinity ligand.
86.    A method for identifying an agent which binds to a protein comprising an amino  
acid sequence of SEQ ID NO:49 or SEQ ID NO:53, comprising the steps of  
10    contacting the agent with the isolated protein under conditions appropriate for  
binding of the agent to the isolated protein, and detecting a resulting agent-  
protein complex.
87.    The method of Claim 86 wherein the step of contacting the agent with isolated  
protein is performed in an artificial membrane system.
- 15    88.    The method of Claim 86 wherein the isolated protein is in isolated plasma  
membrane.
89.    A method for identifying an agent which inhibits interaction between an isolated  
protein comprising amino acid sequence SEQ ID NO:49, or SEQ ID NO:53, and  
further comprising a ligand of said protein, comprising:  
20    (a)    combining:  
         (1)    said isolated protein;  
         (2)    the ligand of said protein; and

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- (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between the said protein of (1) and the ligand of (2);
- 5 (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same
- 10 conditions appropriate for interaction of said protein of (1) with the ligand of (2);
- wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction
- 15 between said protein and the ligand of said protein.
90. The method of Claim 89 wherein (a) is performed in an artificial membrane system.
91. The method of Claim 89 wherein said isolated protein is in isolated plasma membrane.
- 20 92. A method for identifying an agent which binds to a protein, said protein encoded by (1) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48 under high stringency conditions,
- 25 or by (2) a polynucleotide comprising a nucleotide sequence which encodes a



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naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:52 under high stringency conditions, comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

93. The method of Claim 92 wherein the step of contacting the agent with the isolated protein is performed in an artificial membrane system.
94. The method of Claim 92 wherein the isolated protein is in isolated plasma membrane.
95. A method for identifying an agent which inhibits interaction between (1) an isolated protein, said protein being encoded by (i) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48 under high stringency conditions, or by (ii) a polynucleotide having a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:52 under high stringency conditions and (2) a ligand of said protein, comprising:
- (a) combining:
    - (1) said isolated protein;
    - (2) the ligand of said protein; and

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- (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between said protein of (1) and the ligand of (2);
- 5 (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same
- 10 conditions appropriate for interaction of said protein of (1) with the ligand of (2);
- wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction
- 15 between said protein and the ligand of said protein.
96. The method of Claim 95 wherein (a) is performed in an artificial membrane system.
97. The method of Claim 95 wherein said isolated protein is in isolated plasma membrane.
- 20 98. A method for identifying an agent which binds to a protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:49, or SEQ ID NO:53 comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions

appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

99. The method of Claim 98 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.
- 5 100. The method of Claim 98 wherein the isolated protein is in isolated plasma membrane.
101. A method for identifying an agent which inhibits interaction between (i) an isolated protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 90% amino acid  
10 sequence similarity with the amino acid sequence in SEQ ID NO:49, or (ii) a protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 90% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53 and a ligand of said protein, said method comprising:
- 15 (a) combining:
- (1) said isolated protein;
- (2) the ligand of said protein; and
- (3) a candidate agent to be assessed for its ability to inhibit  
20 interaction between said protein of (1) and the ligand of (2),  
under conditions appropriate for interaction between the said  
protein of (1) and the ligand of (2);
- (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which  
25 interaction of said protein of (1) and the ligand of (2) occurs in the

absence of the candidate agent to be assessed and under the same conditions appropriate for interaction of said protein of (1) with the ligand of (2);

5 wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction between said protein and the ligand of said protein.

102. The method of Claim 101 wherein (a) is performed in an artificial membrane system.

10 103. The method of Claim 101 wherein said isolated protein is in isolated plasma membrane.

104. A method for identifying an agent which is an inhibitor of fatty acid uptake by (i) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein consisting of the amino acid sequence in SEQ ID  
15 NO:49, or by (ii) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein consisting of the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
- 20 b) measuring uptake of the fatty acid in the test cells; and
- c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;

wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty  
25 acid uptake by said protein.

105. An inhibitor of fatty acid uptake identified by the method of Claim 104.
106. The method of Claim 104 further comprising the steps of:
- a) administering the agent to one or more test animals;
  - b) measuring exogenously supplied fatty acids in one or more samples of  
5 tissue or bodily fluid from said test animals;
  - c) measuring exogenously supplied fatty acids in one or more comparable  
samples of tissue or bodily fluid from suitable control animals;
  - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is  
10 an inhibitor of said protein.
107. An inhibitor of fatty acid uptake identified by the method of Claim 106.
108. A method for identifying an agent which is an inhibitor of fatty acid uptake by a  
protein, said protein encoded by (i) a polynucleotide comprising a nucleotide  
sequence which encodes a naturally occurring allelic variant of a polypeptide  
15 consisting of the amino acid sequence of FATP2, wherein said polynucleotide  
hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48  
under high stringency conditions, or by (ii) a polynucleotide comprising a  
nucleotide sequence which encodes a naturally occurring allelic variant of a  
polypeptide consisting of the amino acid sequence of FATP4, wherein said  
20 polynucleotide hybridizes to a complement of a polynucleotide consisting of  
SEQ ID NO:52 under high stringency conditions, comprising the steps of:
- a) maintaining test cells expressing said polynucleotide in the presence of a  
fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
  - b) measuring uptake of the fatty acid in the test cells; and

- c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;

wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.

109. An inhibitor of fatty acid uptake identified by the method of Claim 108.

110. The method of Claim 108 further comprising the steps of:

- a) administering the agent to one or more test animals;  
b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;  
c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;  
d) comparing the fatty acids of b) with the fatty acids of c);

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

111. An inhibitor of fatty acid uptake identified by the method of Claim 110.

112. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein being encoded by (i) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:49 or by (ii) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
- b) measuring uptake of the fatty acid in the test cells; and
- c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;

5

wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.

113. An inhibitor of fatty acid uptake identified by the method of Claim 112.

10 114. The method of Claim 112 further comprising the steps of:

- a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
- d) comparing the fatty acids of b) with the fatty acids of c);

15

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

115. An inhibitor of fatty acid uptake identified by the method of Claim 114.

20 116. A method for identifying an agent which is an inhibitor of (i) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein comprising the amino acid sequence in SEQ ID NO:49 or (ii) a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein comprising the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- 5 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- 10 (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

117. The method of Claim 116 further comprising the steps of:
- a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- 15 c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

- 20 118. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by (i) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP2, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:48 under high
- 25 stringency conditions, or by (ii) a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide



consisting of the amino acid sequence of FATP4, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:52 under high stringency conditions, comprising the steps of:

- 5 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- 10 (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

119. The method of Claim 118 further comprising the steps of:

- 15 a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- 20 d) comparing the fatty acids of b) with the fatty acids of c);

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

120. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by (i) a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid  
25 sequence similarity with the amino acid sequence in SEQ ID NO:49 or by (ii) a

nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53, comprising the steps of:

- 5 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- 10 (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

121. The method of Claim 120 further comprising the steps of:

- 15 a) administering the agent to one or more test animals;
- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- 20 d) comparing the fatty acids of b) with the fatty acids of c).

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

122. A method for identifying an agent which binds to a protein comprising an amino acid sequence of SEQ ID NO:57, comprising the steps of contacting the agent  
25 with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

123. The method of Claim 122 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.
124. The method of Claim 122 wherein the isolated protein is in isolated plasma membrane.
- 5 125. A method for identifying an agent which inhibits interaction between an isolated protein comprising an amino acid sequence of SEQ ID NO:57, and further comprising a ligand of said protein, comprising:
- (a) combining:
- 10 (1) said isolated protein;
- (2) the ligand of said protein; and
- (3) a candidate agent to be assessed for its ability to inhibit interaction between said protein of (1) and the ligand of (2), under conditions appropriate for interaction between the said protein of (1) and the ligand of (2);
- 15 (b) determining the extent to which said protein of (1) and the ligand of (2) interact; and
- (c) comparing the extent determined in (b) with the extent to which interaction of said protein of (1) and the ligand of (2) occurs in the absence of the candidate agent to be assessed and under the same
- 20 conditions appropriate for interaction of said protein of (1) with the ligand of (2);
- wherein if the extent to which interaction of said protein of (1) and the ligand of (2) occurs is less in the presence of the candidate agent than in the absence of the candidate agent, the candidate agent is an agent which inhibits interaction
- 25 between said protein and the ligand of said protein.

126. The method of Claim 125 wherein (a) is performed in an artificial membrane system.
127. The method of Claim 125 wherein said isolated protein is in isolated plasma membrane.
- 5 128. A method for identifying an agent which binds to a protein, said protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, comprising the steps of isolating the protein, contacting the agent with the  
10 isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.
129. The method of Claim 128 wherein the step of contacting the agent with the isolated protein is performed in an artificial membrane system.
- 15 130. The method of Claim 128 wherein the isolated protein is in isolated plasma membrane.
131. A method for identifying an agent which inhibits interaction between (1) an isolated protein, said protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said  
20 polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, and (2) a ligand of said protein, comprising:

- (a) combining:
- (1) said isolated protein;
  - (2) the ligand of said protein; and
  - (3) a candidate agent to be assessed for its ability to inhibit
- 5 interaction between said protein of (1) and the ligand of (2),  
under conditions appropriate for interaction between said protein  
of (1) and the ligand of (2);
- (b) determining the extent to which said protein of (1) and the ligand of (2)  
interact; and
- 10 (c) comparing the extent determined in (b) with the extent to which  
interaction of said protein of (1) and the ligand of (2) occurs in the  
absence of the candidate agent to be assessed and under the same  
conditions appropriate for interaction of said protein of (1) with the  
ligand of (2);
- 15 wherein if the extent to which interaction of said protein of (1) and the ligand of  
(2) occurs is less in the presence of the candidate agent than in the absence of the  
candidate agent, the candidate agent is an agent which inhibits interaction  
between said protein and the ligand of said protein.
132. The method of Claim 131 wherein (a) is performed in an artificial membrane  
20 system.
133. The method of Claim 131 wherein the isolated protein is in isolated plasma  
membrane.
134. A method for identifying an agent which binds to a protein encoded by a nucleic  
acid encoding a fatty acid transport protein consisting of an amino acid sequence  
25 sharing at least about 95% amino acid sequence similarity with the amino acid

sequence in SEQ ID NO:57 comprising the steps of isolating the protein, contacting the agent with the isolated protein under conditions appropriate for binding of the agent to the isolated protein, and detecting a resulting agent-protein complex.

- 5    135.    The method of Claim 134 wherein the step of contacting the agent with isolated protein is performed in an artificial membrane system.
136.    The method of Claim 134 wherein the isolated protein is in isolated plasma membrane.
137.    A method for identifying an agent which inhibits interaction between an isolated  
10    protein encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 90% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57 and a ligand of said protein, said method comprising:
- 15    (a)    combining:
- (1)    said isolated protein;
- (2)    the ligand of said protein; and
- (3)    a candidate agent to be assessed for its ability to inhibit  
         interaction between said protein of (1) and the ligand of (2),  
         under conditions appropriate for interaction between the said  
20    protein of (1) and the ligand of (2);
- (b)    determining the extent to which said protein of (1) and the ligand of (2)  
         interact; and
- (c)    comparing the extent determined in (b) with the extent to which  
25    interaction of said protein of (1) and the ligand of (2) occurs in the  
         absence of the candidate agent to be assessed and under the same

conditions appropriate for interaction of said protein of (1) with the  
ligand of (2);

wherein if the extent to which interaction of said protein of (1) and the ligand of  
(2) occurs is less in the presence of the candidate agent than in the absence of the  
candidate agent, the candidate agent is an agent which inhibits interaction  
between said protein and the ligand of said protein.

138. The method of Claim 137 wherein (a) is performed in an artificial membrane  
system.

139. The method of Claim 137 wherein said isolated protein is in isolated plasma  
membrane.

140. A method for identifying an agent which is an inhibitor of fatty acid uptake by a  
protein encoded by a polynucleotide comprising a nucleotide sequence which  
encodes a protein consisting of the amino acid sequence in SEQ ID NO:57,  
comprising the steps of:

- a) maintaining test cells expressing said polynucleotide in the presence of a  
fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
- b) measuring uptake of the fatty acid in the test cells; and
- c) comparing uptake of the fatty acid in the test cells with uptake of the  
fatty acid in suitable control cells;

wherein lower uptake of the fatty acid in the test cells compared to uptake of the  
fatty acid in the control cells is indicative that the agent is an inhibitor of fatty  
acid uptake by said protein.

141. An inhibitor of fatty acid uptake identified by the method of Claim 140.

142. The method of Claim 140 further comprising the steps of:
- a) administering the agent to one or more test animals;
  - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
  - 5 c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
  - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
- 10 143. An inhibitor of fatty acid uptake identified by the method of Claim 142.
144. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide
- 15 hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, comprising the steps of:
- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
  - b) measuring uptake of the fatty acid in the test cells; and
  - 20 c) comparing uptake of the fatty acid in the test cells with uptake of the fatty acid in suitable control cells;
- wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.
- 25 145. An inhibitor of fatty acid uptake identified by the method of Claim 144.



146. The method of Claim 144 further comprising the steps of:
- a) administering the agent to one or more test animals;
  - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
  - 5 c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
  - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
- 10 147. An inhibitor of fatty acid uptake identified by the method of Claim 146.
148. A method for identifying an agent which is an inhibitor of fatty acid uptake by a protein, said protein being encoded by a nucleic acid encoding a fatty acid transport protein comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57,
- 15 comprising the steps of:
- a) maintaining test cells expressing said polynucleotide in the presence of a fatty acid and an agent to be tested as an inhibitor of fatty acid uptake;
  - b) measuring uptake of the fatty acid in the test cells; and
  - c) comparing uptake of the fatty acid in the test cells with uptake of the
- 20 fatty acid in suitable control cells;
- wherein lower uptake of the fatty acid in the test cells compared to uptake of the fatty acid in the control cells is indicative that the agent is an inhibitor of fatty acid uptake by said protein.
149. An inhibitor of fatty acid uptake identified by the method of Claim 148.

150. The method of Claim 148 further comprising the steps of:
- a) administering the agent to one or more test animals;
  - b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from said test animals;
  - 5 c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals;
  - d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.
- 10 151. An inhibitor of fatty acid uptake identified by the method of Claim 150.
152. A method for identifying an agent which is an inhibitor of a protein encoded by a polynucleotide comprising a nucleotide sequence which encodes a protein comprising the amino acid sequence in SEQ ID NO:57, comprising the steps of:
- 15 (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
  - (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
  - (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
  - 20 (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;
- wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.
153. The method of Claim 152 further comprising the steps of:
- 25 a) administering the agent to one or more test animals;

- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- 5 d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

154. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by a polynucleotide comprising a nucleotide sequence which
- 10 encodes a naturally occurring allelic variant of a polypeptide consisting of the amino acid sequence of FATP6, wherein said polynucleotide hybridizes to a complement of a polynucleotide consisting of SEQ ID NO:56 under high stringency conditions, comprising the steps of:
- (a) introducing into host cells one or more vectors comprising a
- 15 polynucleotide expressing said protein;
- (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- 20 (d) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells;
- wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

155. The method of Claim 154 further comprising the steps of:
- 25 a) administering the agent to one or more test animals;

- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- 5 d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

156. A method for identifying an agent which is an inhibitor of a protein, said protein being encoded by a nucleic acid encoding a fatty acid transport protein

10 comprising an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57, comprising the steps of:

- (a) introducing into host cells one or more vectors comprising a polynucleotide expressing said protein;
- 15 (b) culturing a first aliquot of the host cells with fatty acid substrate of said protein and with an agent being tested as an inhibitor of said protein;
- (c) culturing a second aliquot of the host cells with fatty acid substrate of said protein;
- (d) measuring, in the first and second aliquots, uptake of the fatty acid
- 20 substrate of the host cells;
- wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of said protein.

157. The method of Claim 156 further comprising the steps of:

- a) administering the agent to one or more test animals;
- 25 b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;

- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- d) comparing the fatty acids of b) with the fatty acids of c).

whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

158. A method for identifying an agent which is an inhibitor of a fatty acid transport protein, comprising the steps of:

- (a) introducing into cells one or more vectors comprising a gene encoding a cell surface protein and a nucleic acid encoding the fatty acid transport protein;
- (b) contacting the host cells with anti-cell surface protein antibody and labeled fatty acid substrate of the fatty acid transport protein;
- (c) contacting a first aliquot of the host cells with an agent being tested as an inhibitor of the fatty acid transport protein, while leaving a second aliquot of the host cells uncontacted with the agent;
- (d) identifying, in the first and second aliquots, the host cells expressing the cell surface protein by detecting the anti-cell surface protein antibody bound to the host cells; and
- (e) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells identified as expressing the cell surface protein;

wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of the fatty acid transport protein.

159. The method of Claim 158 wherein the host cells regulably express the FATP4 gene.

160. The method of Claim 158 wherein the host cells are prokaryotes.
161. The method of Claim 158 wherein the prokaryotes are *E. coli*.
162. The method of Claim 158 wherein the fatty acid is a radioactively labeled fatty acid.
- 5 163. A method for identifying an agent which is an inhibitor of FATP4, comprising the steps of:
- (a) introducing into cells one or more vectors comprising a gene encoding a cell surface protein and a nucleic acid encoding FATP4;
  - (b) contacting the host cells with anti-cell surface protein antibody and  
10 labeled fatty acid substrate of FATP4;
  - (c) contacting a first aliquot of the host cells with an agent being tested as an inhibitor of FATP4, while leaving a second aliquot of the host cells uncontacted with the agent;
  - (d) identifying, in the first and second aliquots, the host cells expressing the  
15 cell surface protein by detecting the anti-cell surface protein antibody bound to the host cells; and
  - (e) measuring, in the first and second aliquots, uptake of the fatty acid substrate of the host cells identified as expressing the cell surface protein;
- 20 wherein less uptake of the fatty acid substrate in the first aliquot compared to the second aliquot is indicative that the agent is an inhibitor of FATP4.
164. The method of Claim 163 further comprising the steps of:
- a) administering the agent to one or more test animals;

- b) measuring exogenously supplied fatty acids in one or more samples of tissue or bodily fluid from suitable control animals;
- c) measuring exogenously supplied fatty acids in one or more comparable samples of tissue or bodily fluid from suitable control animals; and
- 5 d) comparing the fatty acids of b) with the fatty acids of c);
- whereby, lower fatty acids in step b) than in step c) is indicative that the agent is an inhibitor of said protein.

165. The method of Claim 163 wherein the cell surface protein is CD2.

166. The method of Claim 163 wherein the fatty acid substrate is BODIPY-labeled.

- 10 167. A method for detecting, in a sample of cells, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:48, comprising:
- a) purifying nucleic acid from the cells;
- b) hybridizing 1) purified nucleic acid from the cells to 2) purified nucleic acid comprising SEQ ID NO:48, under conditions that allow
- 15 hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
- c) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule comprising at
- 20 least about 90% sequence similarity to SEQ ID NO:48, has been detected.

168. A method for detecting, in a sample of purified nucleic acid, a nucleic acid molecule having at least about 90% sequence similarity to SEQ ID NO:48, comprising:

- a) hybridizing 1) the sample of purified nucleic acid to 2) purified nucleic acid comprising SEQ ID NO:48, under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
- 5 b) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:48, has been detected.
- 10 169. A method for identifying (1) nucleic acid molecules in fixed cells which specifically interact with a (2) nucleic acid molecule comprising the nucleotide sequence in SEQ ID NO:48, said method comprising the steps of:
- a) adding to the fixed cells the nucleic acid molecule comprising a nucleotide sequence in SEQ ID NO:48;
- 15 b) incubating the fixed cells under conditions allowing hybridization of (1) with (2);
- c) removing the nucleic acid molecule of step a) that has not hybridized; and
- d) detecting hybrid molecules comprising (1) and (2).
- 20 170. A method for detecting FATP2 in a sample of cells, comprising the steps of adding an agent that specifically binds to FATP2 to the sample, and detecting agent specifically bound to the FATP2.
171. The method of Claim 170 wherein the agent is an antibody which binds to FATP2.



172. A method for detecting FATP2 in a sample of cell lysate, comprising the steps of adding an agent that specifically binds to FATP2 to the sample, and detecting agent specifically bound to the FATP2.
- 5 173. The method of Claim 172 wherein the agent is an antibody which binds to FATP2.
174. An isolated antibody which binds to a polypeptide having an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:49.
- 10 175. An isolated antibody which binds to a fatty acid transport protein having the amino acid sequence in SEQ ID NO:49.
176. A method for detecting, in a sample of cells, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:52, comprising:
- 15 a) purifying nucleic acid from the cells;
- b) hybridizing 1) purified nucleic acid from the cells to 2) purified nucleic acid comprising SEQ ID NO:52, under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
- 20 c) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule having at least about 90% sequence similarity to SEQ ID NO:52, has been detected.

177. A method for detecting, in a sample of purified nucleic acid, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:52, comprising:
- 5 a) hybridizing 1) the sample of purified nucleic acid to 2) purified nucleic acid comprising SEQ ID NO:52, under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
- 10 b) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule having at least about 90% sequence similarity to SEQ ID NO:52, has been detected.
178. A method for identifying (1) nucleic acid molecules in fixed cells which specifically interact with a (2) nucleic acid molecule comprising the nucleotide sequence in SEQ ID NO:52, said method comprising the steps of:
- 15 a) adding to the fixed cells the (2) nucleic acid molecule comprising a nucleotide sequence in SEQ ID NO:52;
- b) incubating the fixed cells under conditions allowing hybridization of (1) with (2);
- 20 c) removing the nucleic acid molecule of step a) that has not hybridized; and
- d) detecting hybrid molecules comprising (1) and (2).
179. A method for detecting FATP4 in a sample of cells, comprising the steps of adding an agent that specifically binds to FATP4 to the sample, and detecting agent specifically bound to the FATP4.
- 25

180. The method of Claim 179 wherein the agent is an antibody which binds to FATP4.
181. A method for detecting FATP4 in a sample of cell lysate, comprising the steps of adding an agent that specifically binds to FATP4 to the sample, and detecting agent specifically bound to the FATP4.
182. The method of Claim 181 wherein the agent is an antibody which binds to FATP4.
183. An isolated antibody which binds to a polypeptide having an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:53.
184. An isolated antibody which binds to a fatty acid transport protein having the amino acid sequence in SEQ ID NO:53.
185. A method for detecting, in a sample of cells, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:56, comprising:
- a) purifying nucleic acid from the cells;
  - b) hybridizing 1) purified nucleic acid from the cells to 2) purified nucleic acid comprising SEQ ID NO:56, under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
  - c) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule having at

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least about 90% sequence similarity to SEQ ID NO:56, has been detected.

186. A method for detecting, in a sample of purified nucleic acid, a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:56, comprising:
- 5
- a) hybridizing 1) the sample of purified nucleic acid to 2) purified nucleic acid comprising SEQ ID NO:56 under conditions that allow hybridization between 1) and 2) if the sequences of 1) and 2) have at least about 90% sequence similarity; and
  - 10 b) detecting resulting hybrid nucleic acids in the hybridization; wherein, if hybrid nucleic acids are detected at a significant level compared to a suitable control hybridization, then a nucleic acid molecule comprising at least about 90% sequence similarity to SEQ ID NO:56 has been detected.
187. A method for identifying (1) nucleic acid molecules in fixed cells which specifically interact with a (2) nucleic acid molecule having the nucleotide sequence in SEQ ID NO:56, said method comprising the steps of:
- 15
- a) adding to the fixed cells the (2) nucleic acid molecule comprising the nucleotide sequence in SEQ ID NO:56;
  - b) incubating the fixed cells under conditions allowing hybridization of (1) with (2);
  - 20 c) removing the nucleic acid molecule of step a) that has not hybridized; and
  - d) detecting hybrid molecules comprising (1) and (2).

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188. A method for detecting FATP6 in a sample of cells, comprising the steps of adding an agent that specifically binds to FATP6 to the sample, and detecting agent specifically bound to the FATP6.
189. The method of Claim 188 wherein the agent is an antibody which binds to  
5 FATP6.
190. A method for detecting FATP6 in a sample of cell lysate, comprising the steps of adding an agent that specifically binds to FATP6 to the sample, and detecting agent specifically bound to the FATP6.
191. The method of Claim 190 wherein the agent is an antibody which binds to  
10 FATP6.
192. An isolated antibody which binds to a polypeptide having an amino acid sequence sharing at least about 95% amino acid sequence similarity with the amino acid sequence in SEQ ID NO:57.
193. An isolated antibody which binds to a fatty acid transport protein having the  
15 amino acid sequence in SEQ ID NO:57.
194. A method for modulating fatty acid uptake of cells in culture, comprising adding one or more agents that modulate fatty acid uptake to cells comprising one or more fatty acid transport proteins.
195. The method of Claim 194 wherein the agent modulates fatty acid uptake by  
20 modulating biosynthesis of one or more fatty acid transport proteins.

196. The method of Claim 195 wherein the agent modulates fatty acid uptake by modulating biosynthesis of FATP6.
197. The method of Claim 196 wherein the agent is an antisense oligonucleotide.
198. A method for inhibiting fatty acid uptake in the small intestine of a mammal,  
5 comprising administering to the mammal a therapeutically effective amount of an agent which is an inhibitor of fatty acid uptake by a fatty acid transport protein in the small intestine of the mammal.
199. The method of Claim 198 wherein the agent is administered orally.
200. The method of Claim 198 wherein the fatty acid transport protein is hsFATP6.
- 10 201. A method for inhibiting fatty acid uptake in cardiac muscle of a human comprising administering to the human a therapeutically effective amount of an agent which is an inhibitor of fatty acid uptake by FATP6.
202. A method for directing an agent to cardiac muscle in a mammal, comprising  
15 administering to the mammal a complex which comprises the substance and a moiety which binds to FATP6.
203. A method for directing an agent to liver in a mammal, comprising administering to the mammal a complex which comprises the substance and a moiety which binds to FATP5.

204. A method for detecting a variant allele of a human FATP gene, comprising:

- a) preparing amplified, purified reference DNA encoding all or a portion of a FATP from a human, and amplified, purified test DNA encoding all or a portion of the FATP from a human to be tested as having a variant allele;
- b) determining whether the reference DNA and test DNA differ in DNA sequence;

wherein, if the test DNA differs in sequence from the reference DNA, the test DNA comprises a variant allele of a human FATP gene.

mmFATP1 1  
mmFATP2 1  
mmFATP3 1  
mmFATP4 1  
mmFATP5 1  
ceFATPa 1  
scFATp 1  
miFATP 1

mmFATP1 64  
mmFATP2 41  
mmFATP3 35  
mmFATP4 1  
mmFATP5 74  
ceFATPa 63  
scFATp 64  
miFATP 35

mmFATP1 126  
mmFATP2 101  
mmFATP3 94  
mmFATP4 8  
mmFATP5 140  
ceFATPa 125  
scFATp 134  
miFATP 94

mmFATP1 195  
mmFATP2 171  
mmFATP3 166  
mmFATP4 56  
mmFATP5 213  
ceFATPa 194  
scFATp 204  
miFATP 164

mmFATP1 265  
mmFATP2 241  
mmFATP3 234  
mmFATP4 125  
mmFATP5 283  
ceFATPa 264  
scFATp 273  
miFATP 223

mmFATP1 336  
mmFATP2 311  
mmFATP3 304  
mmFATP4 196  
mmFATP5 353  
ceFATPa 335  
scFATp 344  
miFATP 295

mmFATP1 406  
mmFATP2 381  
mmFATP3 374  
mmFATP4 266  
mmFATP5 423  
ceFATPa 404  
scFATp 417  
miFATP 365

mmFATP1 473  
mmFATP2 446  
mmFATP3 439  
mmFATP4 333  
mmFATP5 488  
ceFATPa 473  
scFATp 489  
miFATP 423

mmFATP1 544  
mmFATP2 517  
mmFATP3 510  
mmFATP4 504  
mmFATP5 539  
ceFATPa 544  
scFATp 562  
miFATP 494

mmFATP1 611  
mmFATP2 585  
mmFATP3 578  
mmFATP4 471  
mmFATP5 627  
ceFATPa 616  
scFATp  
miFATP 562

Figure 1



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Fig. 2A

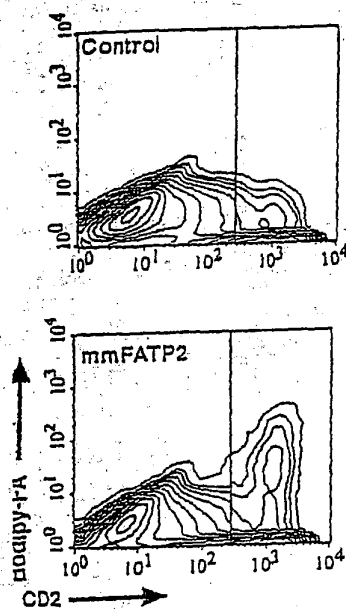


Fig. 2C

Fig. 2B

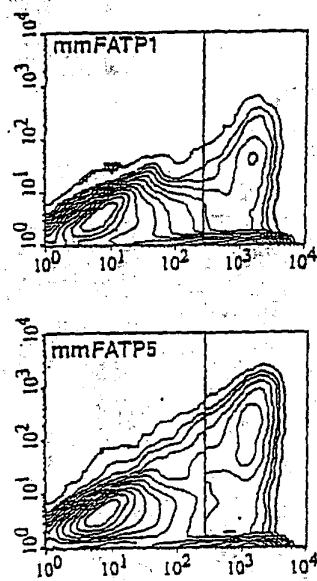


Fig. 2D

Fig. 3

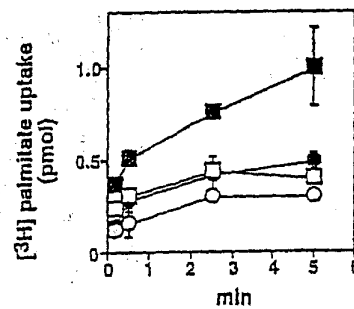
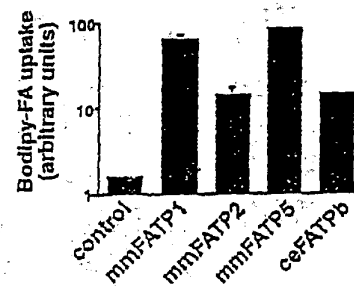


Fig. 4

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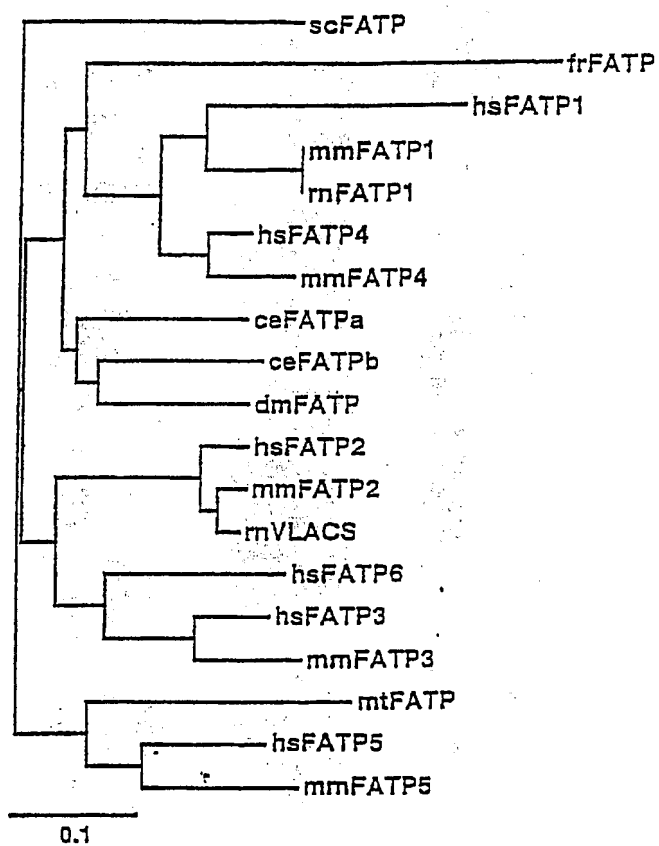


Figure 5

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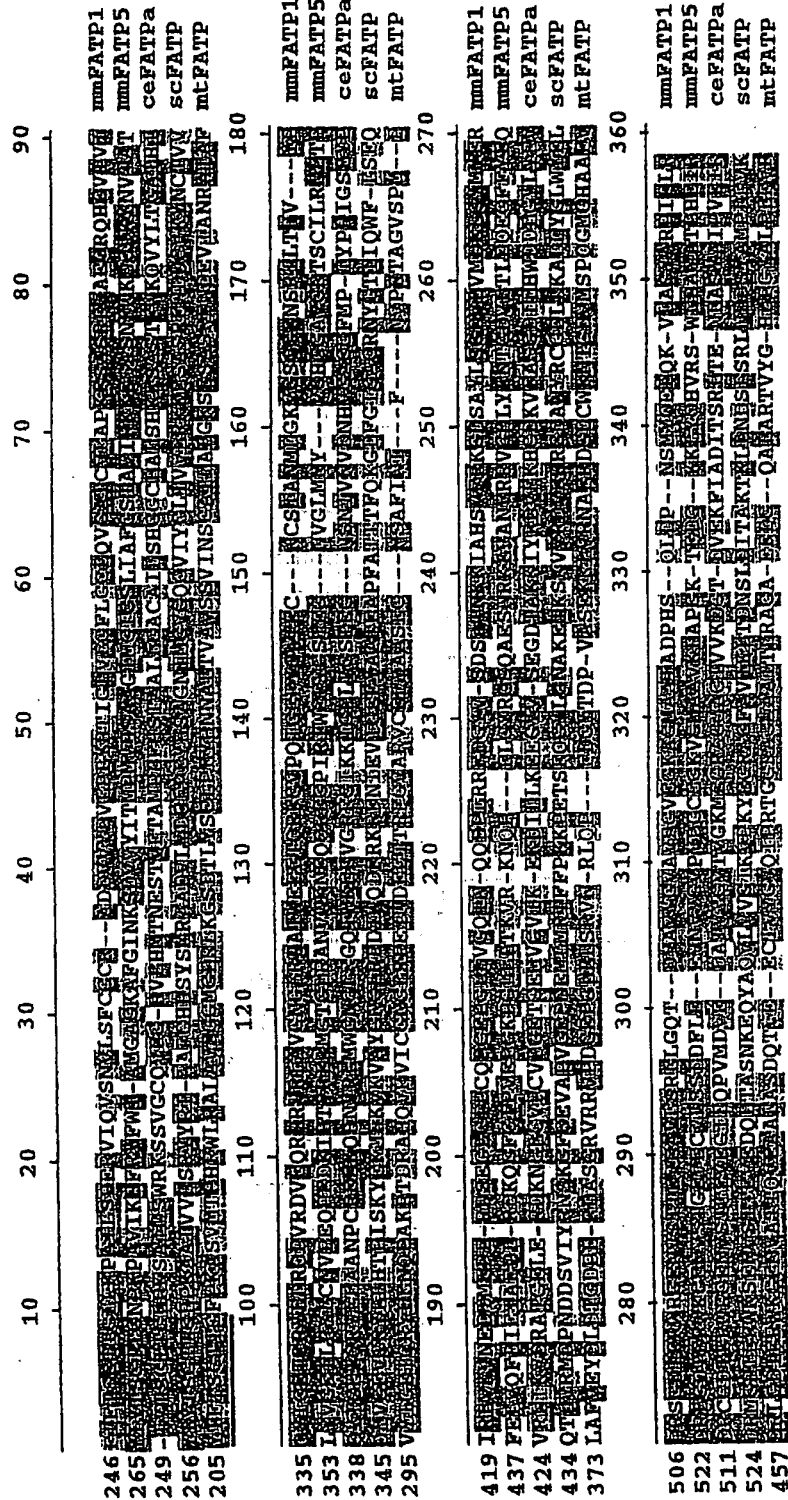


Figure 6

Code	100.0	50.1	100.0	53.3	100.0	51.7	100.0	50.8	100.0	50.4	100.0	50.3	100.0	49.1	100.0	60.3	43.1	100.0	42.3	100.0
nmfATP1	100.0	50.1	100.0	53.3	100.0	51.7	100.0	50.8	100.0	50.4	100.0	50.3	100.0	49.1	100.0	60.3	43.1	100.0	42.3	100.0
nmfATP2	50.1	100.0	53.3	100.0	51.7	100.0	50.8	100.0	50.4	100.0	50.3	100.0	49.1	100.0	60.3	43.1	100.0	42.3	100.0	100.0
nmfATP3	51.8	53.3	100.0	51.7	100.0	50.8	100.0	50.4	100.0	50.3	100.0	49.1	100.0	60.3	43.1	100.0	42.3	100.0	100.0	100.0
nmfATP4	72.6	48.4	51.7	100.0	50.8	100.0	50.4	100.0	50.3	100.0	49.1	100.0	60.3	43.1	100.0	42.3	100.0	100.0	100.0	100.0
nmfATP5	50.2	54.0	51.6	53.0	47.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8
nmfATP1	97.5	49.7	53.0	47.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8	47.8
nmfATP2	50.7	95.2	48.6	47.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8	47.8
nmfATP3	54.1	48.6	47.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	47.8	47.8
nmfATP4	55.7	48.8	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8
nmfATP5	45.5	43.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8
nmfATP1	47.5	47.8	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	47.8	47.8
nmfATP2	47.8	43.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8
nmfATP3	47.8	43.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8
nmfATP4	47.8	43.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8
nmfATP5	47.8	43.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8
nmfATP1	47.8	43.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8
nmfATP2	47.8	43.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2	47.8	48.8	43.2	47.8	45.5	47.5	47.8	43.2	47.8	47.8
nmfATP3	47.8	43.2	46.8	42.3	43.9	47.8	43.2	47.8	48.8	43.2										

Figure 7

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mmFATP3 DNA sequence

ACGACTCAGTATAGGGAGAGAGGCTATGAGGTGGCATGCAC 40  
GGGTAAAGCTTGGGCCCCCTGGAGGGATGCTCTAGAGGGCC 80  
GCGGACCCCGAAAGCTCTGAGAGCGGGTGCAGTCTGGCCT 120  
GGGGTCTGCGGTACCTTGGCCCCGGGAGCAGCGGACACATAC 160  
CTTCTTCATCCACGGGGGGGAGCGCTTTAGCTACGGGGAG 200  
GCTCAGCGGGAGAGCAACGGGATTGCTGGGGCTTTCTGC 240  
GCGCAGCGGGCTGCAACGGGGGGGCGCGGAGGCTGGGGCAG 280  
GGGCAGCACTCAGGAAGGGGCAAGGGTGGGGCTTGGGCT 320  
GGAGATGGGGCTGCTAGAGGGACGAACGGGGCCCCCTCTGG 360  
CAACCGCGCGGCAACGGTGGGGCTGCTGCTCCAGGGGGCC 400

Figure 8A

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GGATTTCCTTTCGATTTCCTTTCGACTGGCCAAAGCTGGC 440  
 CTGGCCAGCGGCTTTCGCTCCACCGCTTTACGCGGAGC 480  
 CCGTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 520  
 CGTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 560  
 CTGCGCGCTTTCGAGCGCTGCTGCTGCTGCTGCTGCTGCT 600  
 CGCGCGCTTTCGAGCGCTGCTGCTGCTGCTGCTGCTGCT 640  
 ATCGCGAGCGAGCGAGCGAGCGAGCGAGCGAGCGAGCGAG 680  
 TACCTTCCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 720  
 ACATCTTCCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 760  
 TCGATTCAGTTCCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 800  
 TACCATCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 840  
 TCGCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 880  
 CATCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 920  
 AAACCTCAAGTTCCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 960  
 AGAACTCAAGTTCCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1000  
 GTGCGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1040  
 TTCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1080  
 GCGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1120  
 TCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1160  
 GTAGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1200  
 GCGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1240  
 CTCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1280  
 ATCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1320  
 CAGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1360  
 CCGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1400  
 CTCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1440  
 ATCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1480  
 TCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1520  
 GCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1560  
 AGCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1600  
 CAGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1640  
 TTCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1680  
 TCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1720  
 ACGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1760  
 GAGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1800  
 GCTTCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1840  
 GCTTCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1880  
 CGCTTCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1920  
 ACCCTTCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1960  
 CATCTTCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2000  
 ATCTGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2040  
 AA 2080  
 AAAAAA 2087

Figure 8B

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## mmFATP3 protein sequence

AADPESSESQCSLAWRLAYLAREQPIHIFLIHGAQRFSYAEERESNRIA 50  
 RAFLRARGWIGGRRGSCRCSTEECARVAPPAGDAAARGITAPPLAFGATV 100  
 ALLLPACPDFLWVWFLAKAGLRFAFVPTALRRGPLLHCLRSOGASALVL 150  
 ATEFLLESLPEPLPALRAMEHLWATGPEINVAGISNLLSEAADQVDEFVP 200  
 GYLSAPQNMIDTCLYIFTSGTTIGLPKAARISHLKVLOOQGFYHLCGVHQE 250  
 DVLYIALPLYHMSGSLIGTVGCLGIGATVVLKPKFSASQFWDDQKRVTL 300  
 VFQYIGELCRYLVNQPPSKAEFDHKVRLAVGSLRPDIWERFLRRFGFLQ 350  
 ILLEHYGMIEGNVATFNITGRQCAVGRASWLYKHIFPFSILIRYDVMIGEPI 400  
 RNAQGHCMITSPGEFGLLVAPVSOQSPFLGYAGAPELAKDKLLKDVFWSG 450  
 DVFFENIGILLVUDEQGFTHFHRTIGDITRWKGENVATTEVAEVLLEILDFL 500  
 QEVNLYGVTVPGHEGRAGMAALAKRPPQALNLVQLYSHVSENLPFYARPR 550  
 FLRLQESLATTETFRQOKVRMANEGFDPSVLSDFLYVLDQDYGAYLELTP 600  
 ARYSALLSGDLRI 613

Figure 9

## mmFATP4 DNA sequence

CCCACGGCTCCGGCCACGGCTCCGGCCATGGCCACGCTGGG 40  
 CGTGGAGGGGGCTCTCATCAACCAACCTTAGGGGGAT 80  
 GCGCTGGCCACGCTCTGACACCTCAAGGCAAGGCTC 120  
 TCATCTTTGGCAGTCATGGGCTCAGCTATCTGTGAGAT 160  
 CCATGCTAGGCTGGAGCCACACTCAGGCTCTTCTGCTCT 200  
 GGATCCTGGGAGCCGACACAGTGGCGGTCAGTACAGAGC 240  
 ATCTGGACCCCTCTCTGCAAGATGCCCCGAGGACCTGGC 280  
 CAGTCACCCAGACAGGGTCTTACAGATAAGCTCTTCTAC 320  
 ATCTACACATCGGGCAACAGGGGCTAACCCTAAGCTGCCA 360  
 TTGTGGGTCACAGCAGGTATTATCGTATGGCTTCCCTGGT 400  
 GTACTATGGATTCCGATCGGGCTGATGACATTGTCTAT 440  
 GACTGGCTCCGCTCTACCACTCAAGCAGTAAACATCGTG 480  
 GGGATTGGCAGTCTTACTTCAAGGCATGACGTGGGAT 520  
 CCGGACAGAGTTCTACGCTCCCGGTTCTGGGATGATTGT 560  
 ATCAAGTACACACTGCACAGTGGTACAGTACATTGGCGAGC 600  
 TCTGGCGCTACCTCTGAAACAGCCACCCCGGTGAGGCTCA 640  
 GTCTGGGCACAAGGTGGGATGGCAGTGGGCAACGGCTC 680  
 CGGCAGTCCATCTGCAACGACTTCTCCAGCGGTTCCACA 720

Figure 10A

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TCCCCAGGTGGCTGAGTTCTATGGGGGCACTGAATGCAA 760  
 CTGTAGCCTGGGCAACTTTGACAGCCGGTGGGGGCGCTGT 800  
 GGCCTCAATAGCCGATCCCTGTCCCTTTGTGTACCCATACC 840  
 GTTTGGTACGTGTCAATGAGGATAACATGCACTGATCCG 880  
 GGGACCCGATGGAGTCTGCATTCCCTGTCAACCAGGTCAG 920  
 CCAGGCGAGCTGGTGGGTCCGATCATCCAGCAGGACCCTC 960  
 TCGCGCGTTTGGACGGGTACCTCAACCAGGGTGGCAACAA 1000  
 CAAGAAGATTGCTAATGATGTCTTCAAGTGGGGGACCAA 1040  
 GCGTACCTTACCTGGTACCTCCCTGGTGTATGATGAGCTGG 1080  
 GTTACCTGTACTTCCGAGATCCGCACTGGGGCACTGTTCCG 1120  
 CTGCAAGGGGCAAGTGTATCTAGCACTGAGGTGGAGGGC 1160  
 ACATCTAGCCCGCTGCTTCATATGGCAGATGTTGGGAGTGT 1200  
 ATGGTGTGAGGGTGGCAGGAACCTGAAGCCCGAGCAGGAT 1240  
 GCGTGGCGTTGCAAGTCCCATCAGCAACTGTGACCTGGAG 1280  
 AGCTTTGACACAGACCTTCAAAAAGTGGCTGCCCTCTGTATG 1320  
 CCGCGCCCATCTTCCCTGGCGTTCTTGGCTGAGCTGCACAA 1360  
 GACAGGGACCTTCAAGTTCCAGACAGAGTTGGCGAAG 1400  
 GAGGGCTTTGACCCATCTGTGTGGAAGACCCGCTGTCTT 1440  
 ATCTGGATGCTGGGAAGGGCTGCTACGTTGCCACTGGACCA 1480  
 GGAGGCCCTATACCCGATCCAGGCAGGGCAGGAGAGCTG 1520  
 TGAATTTCCCGCTACATCCCTCTGAGGGCCAGAGATGCTG 1560  
 GATTTCAGAGCCCTAGCGTCCACCCAGAGGGTCCCTGGGCA 1600  
 ATGCCAGACCAAGCTAGCAGGGCCCGCACCTCCGCCCCCT 1640  
 AGGTGCTGATCTCCCGCTCTCCCAAACTGCCAAGTGACTCA 1680  
 CTGCGCGCTTCCCGGACCCCTCCAGAGGCTTTCTGTGAAAGT 1720  
 CTCATCCAAAGCTGTGTCTTCTGGTCCAGGGGTGGCCCTG 1760  
 GCGCCAGGGTTTCTGATAGGCTCCTTTAGGATGGTATCTT 1800  
 GGGTCCAGGGGGCCAGGGTGTGGGAGAGGAGTACTAAGA 1840  
 TCCCTCCAAATCAGAGGGTGGCTTACAAAGCAACCAAGGCA 1880  
 AAGCCTGTAGACTCAGGAAGCTAAGTGGGCAAGAGCTATA 1920  
 GTGGCCAGTTCATCCCATGTCCACAGAGGATCTTGGTCCAG 1960  
 AGCTGCCAAAGTGTACCTCTCCCTGGCTGCACTCTGGG 2000  
 GAAAGAGGACAGCATGTGGGCACTGGGCACTGTCTCAA 2040  
 GAAGTCAGGATCACACTCAGTCTTGTCTTCTCCAGGTT 2080  
 CCGTTGTCTTGTCTCTGGGGAGGGAGGGACGAGTGTCTG 2120  
 TCTGTCTTCTCTGGCTGTCTGTGAGTCTGTGTGTCTCTC 2160  
 CATCTGTCTTAGCTGAGTGTGGGTGGAAACAGCCATGAGG 2200  
 AGAGTGTGGCTCAGGGGCCAATAAACTCTGCTTGTACTCC 2240  
 TCTTAAAAAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 2280  
 AAAAAAAAAAAAAAAAAAAAAA 2301

Figure 10B



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## mmFATP4 protein sequence

HASAHASCMAKLGVEAALNINLRDAIRHCLDTSKARAL 40  
 IFCSEMASAICEIHASLEPTILSLFCSGSWEPSTVPVSTEH 80  
 LDPLLEDAPKHLPSHPDKGFIDKLFYLYTSGTITGLEKAAI 120  
 VVHSRYYRMASLVYYGFRMRPDDIVYDCLPLYHSSRKERG 160  
 LWQCLLHGMTVWIRKKFSASREWDDCTKYNCITVWQYIGEL 200  
 CRVLLNQPPREAESRHKVRMALGNGLRQSIWIDFSSREHI 240  
 PQVAEFYCATENCSLGNFDSRVGACGENSRILSFVYPIR 280  
 LVRVNEIDIMELIRGEDGVCTPCQPGQPGQLVGRILIQDPL 320  
 RRFDDGYINQGANKKIANVFEKKGDQAVLTGQVLMDELG 360  
 VLYFRDRTEITFRWKGENVSTIEVEGILSRLLHMDVAVY 400  
 GVEVPGIEGRAGMAAVASPTISNCTLESFAQHKKELPLVA 440  
 RPIETLRFLELHKIGIEFKFKTELRKEGFDPSSVVKDPLFY 480  
 LDARKGCYVALDQRAYTRIQAGEEKL 507

Figure 11

## mmFATP5 DNA sequence

CACTCATCAGAGCTAAGAGAGACCTACAGGCTCTCATCTAC 40  
 TTACAGAAAGAGCCCAATGCCATGGGATTTTGAAGAAACTA 80  
 ACGTTACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 120  
 AGCCCCCATGGCCAGCAGCTATGGCTCTGCGCCCTGCGTTG 160  
 GTTCTGCGGAGACCCACATGCCCTTGCTGCTGCTGCTGCTG 200  
 GCACTGCTGCGGACACCCCTGCACTACCTGCTGCTGCTGCTG 240  
 ACTGCTGCTGAGCCCTGCTGCTGCTGCTGCTGCTGCTGCTG 280  
 ATTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 320  
 AAAGATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 360  
 TAAAGTTCAGGCGAGCCCTTAAACAAACATCTCTCAGAGAC 400  
 CTTTGTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 440  
 GACCGGGTGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 480  
 CAATCACAATAAGCCAGCTGCTGCTGCTGCTGCTGCTGCTG 520  
 AGCATGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 560  
 CAGTACACAAGCATGCTGCTGCTGCTGCTGCTGCTGCTGCT 600  
 CCAAGTACATTTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 640  
 CAAGTGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 680  
 CGAGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 720  
 CCAGTGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 760  
 CGAGTGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTG 800

Figure 12A

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TGCCTTCCTACCTTGGCCACAGCTCACCCACCCCGGCTAGTAG 840  
AGGCTCTCTGGGAGCTTCCCTGGATGCTGCTACCTTCTGACCC 880  
AGTACCTTGGGAGCTTCCAGCTACGATTAAAGTGGAAATCT 920  
CCTGCCATATTTCATCTTTACTTTCAGGCACTTCTGCACTCC 960  
CAAAGCCAGCCATCTTTATCATTGAGGGGGTCATACAAGT 1000  
GAGCAAGCTGGCTGCTCTCTCTGCTGATGCTGCTGCTGCTGCT 1040  
GCTGCTCTATGAGCTTCTACCTTCTCTGCTGCTGCTGCTGCT 1080  
TTGCTCTCTGCTGCTTCTGCTGCTGCTGCTGCTGCTGCTGCT 1120  
CTGCTGCTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1160  
GCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1200  
TGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1240  
AACCAGAGACAACTATCATACAGTGGCTGCTGCTGCTGCTGCT 1280  
ACTGGCTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1320  
GCTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1360  
AGAGGGCAATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1400  
GGGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1440  
CTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1480  
GCTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1520  
CCAGCAAAAGCCAGCTTCTGCTGCTGCTGCTGCTGCTGCTGCT 1560  
AACAACCTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1600  
CAATGGCAAACTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1640  
CTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1680  
AAGGCTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1720  
CCGGTGGCAAGGGCGAAAGCTATCTGCTGCTGCTGCTGCTGCTGCT 1760  
TGCTGCTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1800  
TCTATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1840  
CATGGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1880  
GGGCAAGCTATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1920  
CCTATGGCAACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 1960  
GGAGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2000  
GCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2040  
TCTACATACCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2080  
GATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2120  
AATCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2160  
TCTAGAGCTTCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2200  
GCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2240  
CTTGAATGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT 2277

Figure 12B

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## mmFATP5 protein sequence

MALALRWFLGDPICLVLLGLALLGRFWISSWMPHWSLVG 40  
 AALITLFLPLQPPFGLFWLHKDVAFTFKMLFYGLKFRRL 80  
 NKHPPEIFVDALERQALAWPDRVALVCTGSEGSSTINSQ 120  
 DARSCQAAMWLKAKLKDAVIGNIRDAATILVLPSTKISAL 160  
 SVFLGLAKLGFVAMINPHSRGMPLIHSVRSSGASVLIVD 200  
 PDLOENLEEVLPKLLAENIHCFYLGHSSTPGVEALCASL 240  
 DAAPSDFPVPSLRATIKWKSPAIFIFTSGITGLPKPATLS 280  
 HERVIQVSNVLSFGGRADWVYDVLPLYHTTGLVIGFLG 320  
 CLQVATCVLAPKFSASREWAECRQHGVTIVLYVGEILFY 360  
 LCNVPEQPELKIHLVRLAMGTGLRANWKNFQCRFGPIRI 400  
 WEFYGSTEGAWGLMNYVGHOGAVGRITSCILRMUTPEELVQ 440  
 FDIETAEPLRDKQCFCLFVEPKFGILLIKVRKNQPTLGY 480  
 RGSQAESNRKLVANWRRVGDLYFNIGDVLITDQEGFTYFQ 520  
 DRLGDTFRWKGENVSTIGEVECVLSSLDLEEVNIVGVFVP 560  
 GCEGKVGMAAVKLAPGKTFDQKLYQHVRSLPAYATEHF 600  
 IRIQDSLETTINIKLVKSRLVREGFDVGLIADPLYILLNK 640  
 AQIFRSIMFDIVYQAVCEGIWNL 663

Figure 13

## hsFATP2 DNA sequence

ATGGGATTCACICCTTCCTCGACAAAGTGGATGAAGTATC 40  
 AACTGAACCTATUCCAGAGTCATGCGGGTCTGAAGTACT 80  
 TTTTCACICCTTCCTTATACATTTATACCTTCCTGGAACCA 120  
 CAGGTCCTTCCAAAAGCAGCATGATCAGTCATCAGCGCAT 160  
 ATGGATTCGAACCTGGCTTCTTTTGTAGCGGATTCGAAG 200  
 GCAGTGTATGTCATCTATATCAGTCCTGGCTTTTACCACA 240  
 GTGCTGCACTACTGATTCGCAATTCAGGATGTATTGTGGC 280  
 TGGCTGCACTCTTGGCTTGGGACTAAATTTTCAGCGAGC 320  
 CAGTTTGGGATCAGTCGAGAAATACAAAGTCACTGTCA 360  
 TTCAGTATATCGGTCAGCTGCTTGGGTATTTATGCAACTC 400  
 ACCACAGAAACCAATGAAGGATCATAAAGTCAGACTG 440  
 GCACTGGGAAATGGCTTACGAGGAGATGIGIGGCAGACAAT 480  
 TTGTCAGAGATTTGGGGACATATGCATCTATGAGTTCTA 520  
 TGCTGCCACTGAGGCAATATTCGATTTATGAATTATGCG 560  
 AGAAAAGTTGGTGTCTGTGGAAGAGTAAACTACCTACAGA 600  
 AAAAAATCATAACTTATGAACCTGATTAATATGATGTGGA 640  
 GAAAGATCAACCTGTGCGGTATGAAAATGATATTGGGTC 680  
 AGAGTTCCCAAAGGTGAGTTGCACTTCTGGTTTGCAGAAA 720  
 TCACACAACTTACACCATTTAATGGCTATGCTGGAGCAAA 760  
 GGCACACAGAGACAGAAAAACTGACAGATGTCTTTAAG 800

Figure 14A

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AAAGGACACCTCTATTTCAACAGTGGACATCTCTTAATGG 840  
 TTGACCATGAAAATTTTCATCTATTTCCACGACAGATTGG 880  
 AGATACATTCCGGTGGAAAGGGGAAAATGIGGCCACCACT 920  
 GAAGTTGCTGATATAGTTGGACTGGTTGATTTTTTTTCCAA 960  
 GGAAGTAAAATGTTTATGGGAGTGGCATGGGCCAAGATNAT 1000  
 GGAGGTTGCAATTGGCATGGGNTTCCNTTCAAAAATGCAAA 1040  
 GAAAACCATGGAATTTGATGGAAGAAATTTTTTTCAGNAC 1080  
 ATTGCTGATAACCNACCTAGTTATGCAAGGCCCCGGTTTT 1120  
 NTAAGAAACAGGACACCATTTGAGATCAGTGGCAATTTTA 1160  
 AACACCGCAAAATGACCTTTGGTGGAGGAGGCGTTTAACC 1200  
 CNGCTGTCATCAAGATGGCTTGTATTTTCTTTGGATGACA 1240  
 CAGCAAAAATGTATGTGGCTATGACTGAGGCATNTATAA 1280  
 TGCCATAAGTGNTAAAACCTGAAATTTTGAATATTTCCCA 1320  
 GGAGGATAATTTCAACATTTCCAGAAAGAACTGAAATGGAC 1360  
 AGCCACTTGTATATAATCCAACTTTTAAATTTGATTTGAAGATT 1400  
 GTGAGGAAATTTTGTAGGAAATTTGCATACCCGTAAAGGG 1440  
 AGACTTTTTTTAAATAACAGTTTGAGTCTTTTGAAGTAAAAA 1480  
 GATTTAGAGATTATTTATTTTTCAGTGTGCACTTACITGTT 1520  
 GTATTTGCAAACGTAGCTTGTGGAGGCAAGGCATTATTT 1560  
 TTTAAAATACTTAGTAAATTAAGAACACCAACATGTGAA 1600  
 AAAAAAAAAAAAAAAAAAAAAA 1622

Figure 14B

hsFATP2 protein sequence

YIYTSGITGLPKAAMTHQRIWYGIGLTFVSGLKADVIY 40  
 IITLFFYHSAALLIGIHGCTVAGATLALRIKFSASQWDDC 80  
 RKYNVIVIQYIGELLRYLONSPQKENDRDHKVRLALGNEL 120  
 RGDWRQFVKRFGDICTYEFYAITEGNIGFMNYARKVGAV 160  
 GRVNYLQKKITTYDLIKYDVERKDEPVRDENGVCVRVPEGE 200  
 VGLLVCKKITQLTPFNGYACAKAQTEKKLRDVFKKGLLYF 240  
 NSGDLIMVITHENFTYFHDRVGEDIFRWKGENWATTEVADIV 280  
 GLVDEF 286

Figure 15

hsFATP3 DNA sequence

CAATTGGGGACCCCCAGGGGCACTGTATGGCCACATCTCC 40  
 AGGTGAGCCAGGGGAAGTTGCTAAAGGATGTCTTCCGGCC 80  
 TGGGGATGTTTTCTTCAACACTGGGGCACTGCTGGGTCGCG 120  
 CATGACCAAGGTTTTCTCCGCTTCCATGATGTACTGAG 160

Figure 16A

ATACCTTTCAGGTGGCAAGGGCAGAAATGTGGGCACAAACCGA 200  
 GGTGGCAGAGGTCCTTCAGGGCCCTAGATTCTTCTTCAGGAG 240  
 GTGAACGCTCTATGGAGTCTACNIGTGGCAGGGCATGAAGGCA 280  
 GGGCTGGCAATGGCAGGCCCTAGTTCTGGGTCCCCCCCCCAGG 320  
 TTTGGACCTTATGTAGCTCTACACCCAGGTGTCTTGAGAAC 360  
 TTGGCACCTTATGGCCGGGCCCCGATTCTCTAGGCTCCAGG 400  
 AGTCTTTTGGGCACCCACAGACACTTTCAAACAGCAGAAAGT 440  
 TOGGATGGCAAAATGAGGGCTTCGACCCCCAGCAACCTGTCT 480  
 GACCCACTGTACGTTCTTGGCAACAGGCTGTAGGTGCGCTACC 520  
 TGGCCCTTCACAACTGGCCGGGTACAGCGCCCTCTCTGGCAGG 560  
 AAACCTTTCGAATCTGAGAACTTCCACACCTGAGGCAACCTG 600  
 AGAGAGCAACTCTGTGGGGGTGGGGCCCGTTGCAGGTGTAC 640  
 TGGGCTGTACAGGATCTTTTCTATACAGAACTGGCGTCA 680  
 CTATTTTGTGAATAAATGTGGCTGGAGCTGATCCAGCTGTCT 720  
 TCTGACCTTACAAAAA 753

Figure 16B

QFGTPRGIVWEHLQVSQKLLKDVFRPGDVFFNIGDLLVC 40  
DDQGFRLRFHDFRIGEDIFRWKSENVATTEVAEVFFALDFLQE 80  
VNVYGVIVPGHEGRAGMAALNLRPFPHALDLMOLYTHVSEN 120  
LPPYARPRFLRLQESLATTETFKOOKVRMANEGEDPSTLS 160  
DPLYVLDQAVGAYLPLUTARYSALLAGNLR 191 F

Figure 17

TCAAGTACAACCTGCCACGATTGTTCATANCATTGGGTGAACCTG 40  
 TGGCGNTACCTTCCTGAACCAAGCCACCGCGGGGAGGCAGAAA 80  
 AOCAGCAACCAGGTTTCGATGGCACTAGGCCAATGGGCTCCG 120  
 CGAGTCCATCTGGACCAACTTTTTCAGCGGCTTCCACATA 160  
 CCCCAGGTGGCTGAGTTTATCGGGGCCACAGAGTGCAACT 200  
 GTAGGCTGGGGCACTTCCACAGCCAGGTGGGGGCGGTGTGG 240  
 TTTCAATAGCGGCATTCCTGCTTTCGTTGATACCCCATCGG 280  
 TTGGTACGCTGTCAACGAGGACACCATGGACGCTGATCCGGG 320  
 GCGCGGACGGCGCTCGCATTTCCCTTCCAGCTAGGTTAGCC 360  
 GGGCCAGCTGGTGGCGCGCATTCATCCAGAAACACCCCTG 400  
 CGCGGCTTCCATGGCTACCTCAACAGGGCGGCCAACAACA 440  
 AGAAGATTGCCAAGGATGTCCTTCAAGAACGGGGCACAGGC 480  
 CTACCTTACTGGTGTATGTGCGGGTGATGCAACAGCTGGC 520

• • •

Figure 18A

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TACCTGTACTTCCGACACCGCACTGGGGACAGGTTCGGCT 560  
 GGAAGGTGAGCAACGCTGCCACCAACCGAGGTGGAAGGCAC 600  
 ACTCAGCGCGCTGCTGGACATGGCTGACGTGGCGGTGTAT 640  
 CGTGTCCAGGTGCCAGCAACCGAGCGCGCGCGCGGTATGG 680  
 CTGCTGTGGCCAGCGCGCACTGGCACTGTGACCTGGGAGC 720  
 GCTTTGCTTAGGTC 734

Figure 18B

hsFATP4 protein sequence

IGELCRYLLNQPPREAFENQHVRLALGNLRQSIWINFSS 40  
 RFHLPQVAEFYCATHCNCSLGNFDSQVGAOGFNSRILSFV 80  
 YPIRLNVRNEDIMEIIRGPDGVCIPQPGEGQOLVGRITQ 120  
 KDPLRRFDGYLNQGANKKIAKIVFKKGDQAYLITGVLM 160  
 DELGYLYFRDRIGDIFRWKGENVSTTEVEGILSRLLIMAD 200  
 VAVYGVENVPGIEG 213

Figure 19

hsFATP5 DNA sequence

CNTCCCTCTTGTACCAAGTCATGGGACCTTTGTGCTTGGCA 40  
 TCCCTCGGCTGCTTACATCTCGGAGCCACCTGTGTCTCGC 80  
 CCCCAGTTCGTCTACCTTCTGCTTCTGCGATGACTGTGCG 120  
 CAGCATGGCGTACAGTTCATCCTGTATGTGGCGGAGCTCC 160  
 TCGCTACCTTGTGTACATTCCCCAGCAACACAGCTACCG 200  
 CACACATACAGTCCGCTGCGCAATGGCGCAATGCACTACCG 240  
 GCTGTATGTGTGCGGAGACCTTCCAGCAGCGTTTCCGTCT 280  
 ATTTCGATCTCINGCGAAGTCTTACCGGCTTCCACAGAGG 320  
 GCAACATGGGCTTTAGTTCACCTATTGTGTGCGGCGCTG 360  
 CCGGCGCGCTGCGGCAAGATGGAGCTTGGCTTCTCTCCAA 400  
 TCGTGTCCCGCTTTCAGCTGGTGCAGTTCGACATGCGGCG 440  
 GCGGTAGCGCTGTGAGGCAATCAGCGCTTCTGCTATCCT 480  
 GTAGCGCTACGGGAGCGCGGCTGCTGTTCACCAAGGTGG 520  
 TAAGCCAGCAACCGCTTGTGGGCTACCGAGGCGCGCGTACA 560  
 GCTGTGCGTAACCGTAAGCTGGTGGCGAAGGTGCGGCAATG 600  
 GCGTACGTTTACTACAAACCGGCGAAGTACTGGCGCATGG 640  
 ACGCTAAGGCTTCTCTACTTCCGCGACCGACTCGGCGCA 680  
 CACCTTCCGATGCTAGCGCGAGAACGTTGTCCACGACGAG 720  
 GTGCGAGCGCGTGTGTGTGCGAGGTGCACTTCTGTCAACAG 760  
 TTAAGGTGTATGGCGTGTGCGGTGCGAGGTGTGTGCGGTAA 800  
 GGTGGCGATGCGCTGTGTGCGCATTAGCGCGCGCGCACT 840

Figure 20A

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TTTCAGCGGGAGAGAGTTGTACAGCAAGTTGGGGTTGGC 880  
 TCGCTGGCTTACGCTACGCGCCATTTCATCGGCATCCAGCA 920  
 CGCCATGCGAGGTCACAGCAAGTTCAAACGTATGACAGCC 960  
 CCGTTGGTGGGTCAGGCGTTCAATGTGGGGATGGTGGTTG 1000  
 ACCCTCTGTTTGTACTGCAACCGGGGGCAGTCCCTTCGG 1040  
 GCGGCTGACCGTACAAATGTACCAGCGCTGTGTGTGAGGCA 1080  
 ACCTGGAGGCTCTATCACCCTGGGCAACCCACTGGGGTAG 1120  
 GCAATCAAAGCCAGCCACCGCCACCGCAACACACTGGGTGT 1160  
 CCGTTTCATCGGGCGGTGTGTGAATCCAGCGCTGGGCAT 1200  
 ACCCTCAACCTCAGTGGCGTGAATGACAGTGGGGCGCTG 1240  
 TAGCAGTGGCAGATAAATCAGMTGYGTTACAGAAA 1278

Figure 20B

hsFATP5 protein sequence

EQHGAIVQLLLGALRGFGKDGACLLRMLSPFELVQEDM 40  
 EAAEFVRDNGFCIFVGLGEFGLLLIKVVSQQPFVGYRGP 80  
 RELSERKLVRNVRQSEIVYNTGEMLAMDRGFLYFRDL 120  
 GDTFRWKGENVSTHEVEGVLSQVDFLOQVNVYGVCPGCE 160  
 KKVGMAAVALAPGQITDGEKLYQHVRAWLPAYATPHFIR 199

Figure 21

hsFATP6 DNA sequence

CCGTTGTGTGTAAAGCAAGAAATTTTCAGCAAGCCAGTTT 40  
 TGCAGTGCATGCAAGAGTATGATGTGACTGTGTGTTTCACT 80  
 ATATTGGAGCACTTTGTGCGTACCTTTGCAACAAATCTAA 120  
 CAGACAAGCAAGAAAGCATCATAAGGTGGGTTTGGCAATT 160  
 CGAAATGGCATACGAGTGTATGATGAGAGAAATTTTATAG 200  
 ACAGATTGTGAAATATAAAGGTGTGTGAACCTTTATGCAGC 240  
 TACCGAATCAAGCATATCTTTTCATGAACCTACAGTGGGAGA 280  
 ATTGGAGCAATTGGGAGCAACAAATTTGTGTTTACAACTTC 320  
 TTTCCACTTTTGTACTTAATAAAGTATGACTTTTCAAGAA 360  
 TGAACCATGCAAAATCAGCAGGTTGGGTAATTCATGAGA 400  
 AAAAGCAGACCTTGTCTTCTCATTCTCTGAGTGAATGCAA 440  
 AAAATCGCTTCTTTGGCTATGCTGGGCTTATAAGCACAC 480  
 AAAAGCAAAATGCTTTGTGATGTTTAAAGAGGGAGAT 520  
 GTTTACCTTAATATCTGAGACTTAATAGTCCAGGTCAGG 560  
 ACAATTTCCTTTATTTTGGGACCGTACTGGAGACACTTT 600  
 CAGATGCAAGAGCAAAATGTGCGCAACCACTGAGGTTGCT 640  
 CATGTATTTGCAATGTGTGATTCATACAGGAGCAACAG 680  
 TCTATGGTGTGGCTATATCAGGTTATGAAGGAGAGCAGG 720

Figure 22A

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AATGGCTTCTATTATTTTAAAACCAAATACATCTTTAGAT 760  
 TTGGAAAAAGTTTATGACAAGTTGTAAACATTTCTAOCAG 800  
 CTTATGCTTGTCCACGATTTTTTAAGAATTCAGGAAAAAAT 840  
 GGAAGCAACAGGAACATTCAAACIATTTGAAGCATCAGTTG 880  
 GTGGACATGCGATTTAATCCACTGAAAATTTCTGAACCAC 920  
 TTTACTTCATGCGATAACTTGAAAAAGTCTTATGTTCTACT 960  
 CACCAGGGAACCTTTATCATCAAATAATGTTAGGGGAAATA 1000  
 AAACCTTTAAGATTTTATATCTAGAACTTTTCATATGCTTT 1040  
 CTTAGGAAGAGTGAGAGGGGGTATATGATTCTTTTATGAA 1080  
 ATGGGGTAAGGGAGCTAACATTAATTATGCAATGTAATA 1120  
 TTTCTTAATAATGAGAGATAATTTTTTAATTGCATAAGAA 1160  
 TTTTAATTTCTTTTAATTGATATAAACAGAGTTGATTATT 1200  
 CTTTTTATCTATTTCGAGATTTCAGTGCATAACTAAGTATT 1240  
 TTCTTAATACTAAAGATTTTAAATAATAAATAGIGGCTA 1280  
 GCGGTTTGGACAATCACTAATAAATGTACTTTCTAATAAGT 1320  
 AAAATTTCTAATTTTGAATAAAAGATTAAATTTTACTGAA 1360  
 A 1361

Figure 22B

hsFATP6 protein sequence

ACVLKKKFSASQFWSDCCKKYDVIVFQYTGELCRYLCKQSKREFEKDKHVR 50  
 LAINGIRSDWREFLLDRFGNLKVCELYAATESSTSEFMNYTGRIGATGR 100  
 NLFYKLLSTFDLIKDYDFQKDEEMRNEQGWEMRKRRLPGLLISRVNAKNPF 150  
 FGYAGFPYKHDKLLCDVFKKGLVYLNIGDLIVQDQDNFLYFWRDRTGDTF 200  
 RWKGENVATTEVADVIGMLDFTQEANVYGVAISGYEGRAGMASTILKENT 250  
 SLDEKVEYEQVVFIFLPAYACPRFLRTQEKMEATGTFTKLLKHQLVEDGFNP 300  
 LKLTSEPLYFMDNLKKSIVLLITRELYDQIMLGENTKL 335

Figure 23

mtFATP DNA sequence

TAGTCGATAACGTCAGGACGGCTCTGCGGGGCGCTCGGCACC 40  
 TTCTGAGGTTGGTTCGACAAGCAATTGACATTTTCGAAA 80  
 CGAATCGAGGGCTTAAGTGTCCGATTACTAAGGGGGGGCA 120  
 CACACAACGGTCAGGCTGATCGACCTGGCAACTCGGATGC 160  
 CGCGAGTGTGTGGGGACACGCGGGGATTTGTGGTGGGGC 200  
 AATGACCGGGGCTGCTGGCGGGCGCGAATTCCAAGGGGTGC 240  
 ATGGGCACGGTGTCCAGGACCGGGGCGGCTCGCTACGGTG 280  
 ACCGAGTCTTCTGAAATTCGGCGATCAGCAGCTGACCTA 320  
 CCGCGACGCTAACGCGACCGGCAACCGGTACGCGGGGGTG 360

Figure 24A



Figure 24B

## mtFATP protein sequence

msdyvggahttvrlidlatmprivladtpvivrgamtgll 40  
anpnskasigtvfgdraarygdrvflkfgdgglttyrdana 80  
tanryaavlaargvgpgdvvgimlmspstvlamlatvkc 120  
gaiagmlryhqrgevlahslglldakvliaesdlvsavae 160  
ogasrgrvagdvltvedverfättapatmpasasavgakd 200  
tafyiftsgttgfpkasvntthhrwlravfiggnglrllkg 240  
sdtlyscplplyhnnaltvavssvinsgatllalgksfsasr 280  
fwdevianrätavfyigeicryllngpakptdrahqvrvi 320  
cnglrpeiwdetttrfgvarvcefyaasegnsafinifn 360  
vprttagvspmplafveydlldtgdpldrdsgrvrvpdgep 400  
glllsrvnrlqpfdytdpvasekdvlvnafrdgdwfnf 440  
gdvmspgomghaafvdrldgtfrwkgenvattqveaalas 480  
dgtveectvygvqiprtgggragmaaitlragaefdgqala 520  
rtvyghlpgyalplfvrvvgsлахттfkarkvelmqay 560  
gadiedplyvlagpdegypyyaeypeevslgmpog 597

Figure 25

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## hsFATP1

1 tcy acc cac ggc gtc cgg gac ccc aaa gca gaa gcc cgc aca gta ggc aca gcy cac cca  
61 aga agy gtc cag gag tct gca gaa aca gaa agy tcc ccy gcc tca gcc tcc tag tcc ccy  
121 ctc gcc tcc tgc ctg agc ttc tgg gag act gaa ggc acy gct tgc agc ttc agy atg cgg  
H R  
181 gct ccy ggc gcy ggc ggc ggc tgc gtc gtc tcy ctc gcy cty tcy tcy cty gcy cty  
A P Q A A G A A S V V S L A L L W L L O L  
241 ccy tgg acc tgg agc gcy gca gcy gcy ctc gcc gtc tgc gtc ggc agc ggc gcy tgg ggc  
P W T W S A A A A L G V Y V G S O O W R  
301 ttc cty cgc atc gtc tgc agc acc gcy agy cga gac ctc ttc ggc ccc tct gtc cty acc  
F L R I V C K T A R R D L F G L S V L I  
361 ccy gtc cgc cty gag cty ccy ccy cac cag cgt gcc ggc cac acc atc ccy cgc atc tct  
R V R L E L R R H O R A G H T I P R I F  
421 cag gcy gta gcy cag cga cag ccc gag cgc cty gcy cty gtc gat gcc ggc acc ggc gag  
Q A V V Q R Q P E R L A L V D A O T O E  
481 tgc tcy acc tct gcy cag cty gac gcc tac tcc aat gcy gta gcc aac ctc ttc cty cag  
C W T F A Q L D A Y S N A V A N L F R O  
541 cty gtc ttc gcy ccy ggc gac gtc gtc gcc atc ttc cty gag ggc ccy ccy gag ttc gtc  
L G F A P G D V V A I F L E G R P E F V  
601 gcy cty tcy cty ggc cty gcc aag gcy ggc atg gag gcc gcy cty ctc aac gcy aac cty  
G L W L Q L A K A G H E A A L L H V N L  
661 ccy ccy gag ccc cty gcc ttc tgc cty ggc acc tcy ggc gtc aag gcc cty acc ttc ggc  
R R E P L A F C L G T S G A K A L I F O  
721 gca gaa atg gtc gcy gtc ggc gaa gcy agc ggc cat cty ggc aag agt cty acc aag  
G E H V A A V A E V S G H L G K S L I X  
781 ttc tgc ttc gga gac tgc ggc ccc gag ggc atc tcy ccy gac acc cag ctc cty gac ccy  
F C S G D L Q P E Q I L P D T H L L D P  
841 cty cty aag gag gcc tct act gcc ccc tcy gca cag acc ccc agc aag ggc atg gac gat  
L L K E A S T A P L A Q I P S K G M D D  
901 cgt ctc ttc tac atc tac agc tcy ggc acc acc ggc cty ccc aag ggc gcc atc ggc cty  
R L F Y I Y T S O T T G L P K A A I V V  
961 cac agc agy tac tct cgc atg gca gcc ttc ggc cac cag gcc tac cgt atg cag gcy gcc  
H S R Y Y R M A A F G H H A Y R H Q A A  
1021 gac gcy ctc tac gac tgc cty ccc cty tac cag tcy gca gga aac atc atc ggc gcy ggc  
D V L Y D C L P L Y H S A G N I I G V G  
1081 cag tct ctc atc tat ggc cty aca gcc gtc ctc cty aag aag ttc tcy gcc agc cgt ttc  
Q C L I Y Q L T V V L R K K F S A S R F  
1141 tcy gac gac tgc atc aag tac aac tgc acy gcy gct cag tac atc ggc gag atc tgc cgc  
W D D C I K Y N C T V V Q Y I O E I C R  
1201 tac cty cty aag cag ccy gcy cgy gag gcy gag agy cga cac cgy gcy cgy cty gcy gcy  
Y L L K Q P V R E A E R R H R V R L A V  
1261 ggc aac ggc cty cgt ctc gcc atc tcy gag gag ttc acy gag cgt ttc ggc gta cgy caa  
G N G L R P A I W E E F T E R F G V R O  
1321 att gcy gag ctc tac gcc gcc acc gag tgc aac tgc agc att gcc aac atg gac ggc aag  
I G E F Y G A T E C N C S I A N H D G K  
1381 gtc gcc ttc tct ggt ttc aac agc cgc atc cty ccc tac gcy tac ccc atc cgy cty gcy  
V G S C G F N S R I L P H V Y P I R L V  
1441 aag gcc aat gag gac aca atg gag cty cty cgy gat gcc cag ggc ctc tgc acc ctc tgc  
K V N E D T H E L L R D A Q G L C I P C  
1501 cag gcc ggc gag ccc gcc ctc ctc gcy gcy cag acc aac caa cag gac ccy cty cgt cgt  
Q A G E P G L L V G Q I N Q Q D P L R R  
1561 ttc gat ggc tat gtc agc gag agc gcc acc agc aag aag atc gcc tac agc gtc ttc agc  
F D G Y V S E S A T S K K I A H S V F S  
1621 aag ggc gac agc gcc tac ctc tca ggc gac gcy cta gty atg gat gag cty ggc tac atg  
X G D S A Y L S G D V L V H D E L G Y H  
1681 tac ttc cgy gac cgt agc ggc gac acc ttc cgt tgy cga ggc gag aac gtc tcc acc acc  
Y F R D R S G D T F R W R G E N V S T T  
1741 gag tcy gag gcy gcy cty agc cgc cty cty ggc cag aca gac gcy gcc gtc tac gcy gcy  
E V E G V L S R L L G O T D V A V Y G V  
1801 gct gtc cta gga gcy gag ggc aag gca ggc atg gcy gcc gcc gca gac ccc cac agc cty  
A V P Q V E G K A G H A A V A D P H S L  
1861 cty gac ccc aac gcy ata tac cag gag cty cgy aag gcy cty gca ccc tat gcc cgy ccc  
L D P N A I Y Q E L Q K V L A P Y A R P  
1921 atc ttc cty cgc ctc cty ccc cag gcy gac acc aca ggc acc ttc aag atc cag aag atc  
I F L R L L P Q V D T T G T F K I Q K T  
1981 agy cty cag cga gag ggc tct gac cca cgc cag acc tca gac cgy ctc ttc ttc cty gac  
R L O R E G F D P R Q T S D R L F F L D  
2041 cty aag cag ggc cac tac cgt ccc tta aat gag gca gtc tac act cgc atc tgc tcy ggc  
L K O G H Y L P L N E A V Y T R I C S G  
2101 gcc ttc gcc ctc tga agc tgc ttc tct act ggc ccc aca ctc cgy gcc tgy tgy gag agy  
A F A L  
2161 cca gct tga gcc aga cag cgc tgc cca gcy gcy gcc gcc tag tac aca ccc acc tgy cgy  
2221 agc tgc acc tgy cac ggc cca tcc tgy act gag aca cty gaa cct cag agy aac cgy tgc  
2281 ctc tct ggc gcc tgy gtc ccc tgc tgc ctc ctc ctc ctc tct tct cag cct cty tct  
2341 ctc tcc atc cct gtc cct gtc tgy cct taa ctc ttc ctc ctc tct tct tct cct tct  
2401 ttc tct tct tct aag ata gag tct cac tct gct gcc cgy gct aga gcy cag tgy tgy gat  
2461 ctc ggc tca cty caa cct cty cct cct ggc gct caa gtc atc ctc cca cct cag cct cct  
2521 ggc tag cty gga tta cag gca ccc gcc acc agc tcc agc taa tct tta tat tct tag tag  
2581 aga cgy ggc ttc acc atg tgy gtc agy cty gtc tgy aac tcc tga cct cag gcy atc cgc  
2641 tgy cct cgy cct ccc aga gty cty gga tta tag gcy tga gcc tct ggc cgy gcc tct cct  
2701 ttc tcc tct cct cct cty cgy aga gty gaa cac agy tgt cct ggc agc tgc atc tgy tgc  
2761 agy gtc cag cty cct tgy ggc act gca gga acc atc tcc cct ggc ccc tgy act cgy act  
2821 ggc ggc ttc cca ccc cct tct cgy cty tgc tct agy gag ccc caa tcc agc cct gty  
2881 gct gtc ggc ttc cag atg cty cag ctc cat gty act tcc aag cag gcc ctc cgc cct ccc  
2941 tgc tga atg gag gag cgy ggc gtc ccc cag gcc aac tgy aaa atc tcc tag gct agy cca  
3001 act gcc ttc tgc act tcc cgy ttc cty tca cat ttc ccc agc ccc acc ttc cct tcc tga  
3061 tgc cct gaa agc ttc cgy aat tga cty tga cca cct gga tct cac cac tgc cag ccc tgy  
3121 cct tga tgc ccc cat tta gcc atc tcc atg gag cty cty cty gag ggc cct gaa ccc tgc  
3181 act gcy tgy cty ccc agc cag cty cct cct gtc cty gga gga ggc ttc cty ggc ttc ttc  
3241 atc tgy tgc ttc tac tgy agy gtc cca cag gag agy cag cag agy ggc cag ggy agy tct  
3301 cct ccy ggc ggt tgy cct ctc aag cct cag ggc ttc tag cct gtc gaa tat acc cca cct  
3361 ggc ggc tgy cct ctc tga tgc ccc cac tga tgy cct tga cac cgt gct ggc ggc gat gtc  
3421 cca gac aac ccc acc agy agy gcc cag aca tcc cta cty gct tcy cty gcy gct cat ctc  
3481 gaa cat cca cgc cag cct ttc tgy ggc cgy cca acc agy cgy cct gtc cgt cty tcc ccc  
3541 ccc cag cag ccc ccc gcc cct gya gcy gcy ggc cca tgy caa gag aca cgy tgy cgt  
3601 ctc atg tga act ttc cty ggc act gty gct tta tct cct aat tga tct aag aca taa acc  
3661 tga aga ccy cct ggc gaa aaa aaa aaa aaa agy gcy gcc gc

Figure 26



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Protein sequence 646 a.a. MPAPGAGAAASVV ... VYTRICSGAFAL

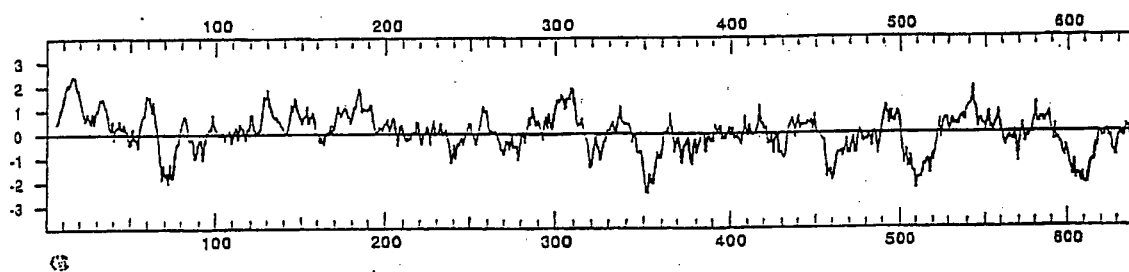


Figure 28A

Protein sequence 646 a.a. MPAPGAGAAASVV ... VYTRICSGAFAL

646 Amino Acids MW : 71062 Dalton

		n	n(%)	MW	MW(4)
A	ala alanine	64	9.9	4946	6.4
C	cys cysteine	15	2.3	1545	2.2
D	asp aspartic acid	30	4.6	3450	4.9
E	glu glutamic acid	31	4.8	4000	5.6
F	phe phenylalanine	29	4.5	4264	6.0
G	gly glycine	63	9.8	3592	5.1
H	his histidine	13	2.0	1781	2.5
I	ile isoleucine	29	4.5	3279	4.6
K	lys lysine	22	3.4	2818	4.0
L	leu leucine	77	11.9	8707	12.3
M	met methionine	11	1.7	1441	2.0
N	asn asparagine	15	2.3	1710	2.4
P	pro proline	29	4.5	2814	4.0
Q	gin glutamine	25	3.9	3201	4.5
R	arg arginine	49	7.6	7648	10.8
S	ser serine	33	5.1	2872	4.0
T	thr threonine	27	4.2	2728	3.8
V	val valine	51	7.9	5052	7.1
W	trp tryptophan	9	1.4	1674	2.4
X	unk unknown	-	-	-	-
Y	tyr tyrosine	24	3.7	3913	5.5
Z	--- STOP	-	-	-	-

Figure 28B

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11

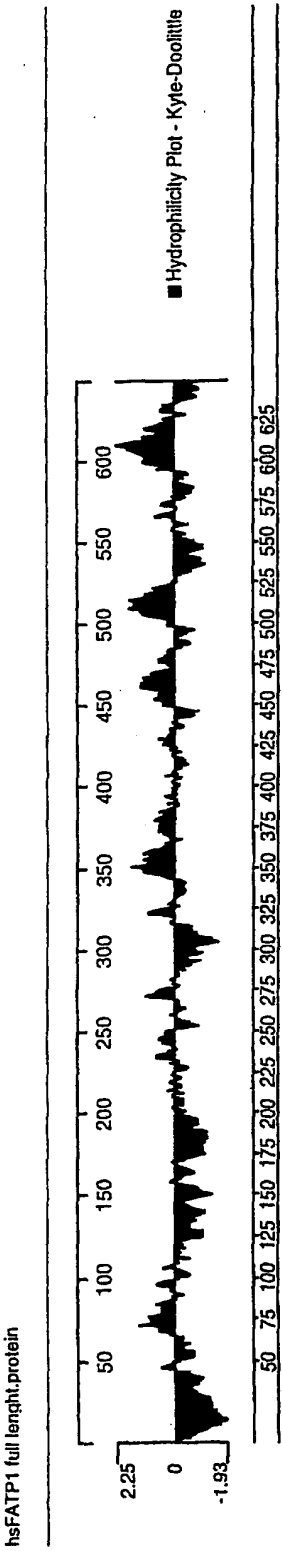


Figure 28C

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hsFATP4.pep -&gt; KD Hydrophobicity &lt;11/1&gt;

Protein sequence 643 a.a. MLIGASLVGVLL ... AYSRIQAGEEKL

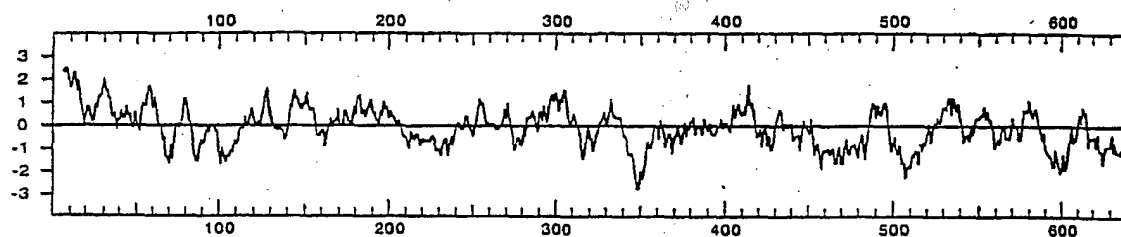


Figure 29A

hsFATP4.pep -&gt; A. A. Usage

Protein sequence 643 a.a. MLIGASLVGVLL ... AYSRIQAGEEKL

643 Amino Acids MW : 72018 Dalton

		n	n(%)	MW	MW(%)	
A	ala	alanine	46	7.2	3267	4.5
C	cys	cysteine	16	2.5	1648	2.3
D	asp	aspartic acid	33	5.1	3795	5.3
E	glu	glutamic acid	33	5.1	4258	5.9
F	phe	phenylalanine	34	5.3	5000	6.9
G	gly	glycine	54	8.4	3079	4.3
H	his	histidine	12	1.9	1644	2.3
I	ile	isoleucine	30	4.7	3392	4.7
K	lys	lysine	31	4.8	3970	5.5
L	leu	leucine	76	11.8	8594	11.9
M	met	methionine	12	1.9	1572	2.2
N	asn	asparagine	21	3.3	2394	3.3
P	pro	proline	31	4.8	3008	4.2
Q	gln	glutamine	23	3.6	2945	4.1
R	arg	arginine	45	7.0	7024	9.8
S	ser	serine	35	5.4	3046	4.2
T	thr	threonine	32	5.0	3233	4.5
V	val	valine	46	7.2	4527	6.3
W	trp	tryptophen	8	1.2	1488	2.1
X	ukw	unknown	-	-	-	-
Y	tyr	tyrosine	25	3.9	4078	5.7
Z	---	STOP	-	-	-	-

Figure 29B

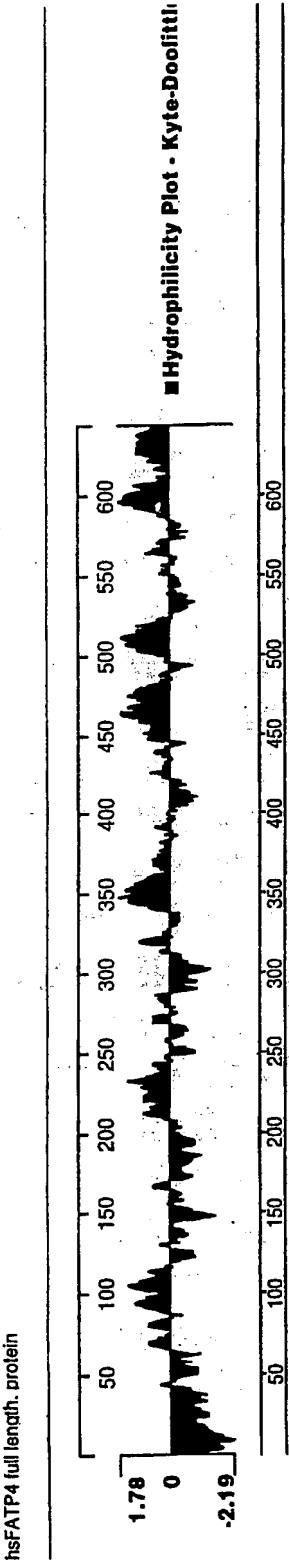


Figure 29C



1 1 hFAT1p1con.seq ORF  
1 mFAT1p1.seq ORF (from genomic)

51 hFAT1p1con.seq ORF  
51 mFAT1p1.seq ORF (from genomic)

101 hFAT1p1con.seq ORF  
101 mFAT1p1.seq ORF (from genomic)

151 hFAT1p1con.seq ORF  
151 mFAT1p1.seq ORF (from genomic)

201 hFAT1p1con.seq ORF  
201 mFAT1p1.seq ORF (from genomic)

251 hFAT1p1con.seq ORF  
251 mFAT1p1.seq ORF (from genomic)

301 hFAT1p1con.seq ORF  
301 mFAT1p1.seq ORF (from genomic)

351 hFAT1p1con.seq ORF  
351 mFAT1p1.seq ORF (from genomic)

401 hFAT1p1con.seq ORF  
401 mFAT1p1.seq ORF (from genomic)

451 hFAT1p1con.seq ORF  
451 mFAT1p1.seq ORF (from genomic)

501 hFAT1p1con.seq ORF  
501 mFAT1p1.seq ORF (from genomic)

551 hFAT1p1con.seq ORF  
551 mFAT1p1.seq ORF (from genomic)

601 hFAT1p1con.seq ORF  
601 mFAT1p1.seq ORF (from genomic)

651 hFAT1p1con.seq ORF  
651 mFAT1p1.seq ORF (from genomic)

701 hFAT1p1con.seq ORF  
701 mFAT1p1.seq ORF (from genomic)

751 hFAT1p1con.seq ORF  
751 mFAT1p1.seq ORF (from genomic)

801 hFAT1p1con.seq ORF  
801 mFAT1p1.seq ORF (from genomic)

851 hFAT1p1con.seq ORF  
851 mFAT1p1.seq ORF (from genomic)

901 hFAT1p1con.seq ORF  
901 mFAT1p1.seq ORF (from genomic)

951 hFAT1p1con.seq ORF  
951 mFAT1p1.seq ORF (from genomic)

1001 hFAT1p1con.seq ORF  
1001 mFAT1p1.seq ORF (from genomic)

1051 hFAT1p1con.seq ORF  
1051 mFAT1p1.seq ORF (from genomic)

1101 hFAT1p1con.seq ORF  
1101 mFAT1p1.seq ORF (from genomic)

1151 hFAT1p1con.seq ORF  
1151 mFAT1p1.seq ORF (from genomic)

1201 hFAT1p1con.seq ORF  
1201 mFAT1p1.seq ORF (from genomic)

1251 hFAT1p1con.seq ORF  
1251 mFAT1p1.seq ORF (from genomic)

1301 hFAT1p1con.seq ORF  
1301 mFAT1p1.seq ORF (from genomic)

Figure 30A



[illegible]

Figure 3/A



Page 1

Alignment Report of Unifed, using ClustalW2.0 with PAM250 matrix

1	1	hsFAT11pep
1	1	mmFAT11pep
61	61	hsFAT11pep
61	61	mmFAT11pep
121	121	hsFAT11pep
121	121	mmFAT11pep
181	181	hsFAT11pep
181	181	mmFAT11pep
241	241	hsFAT11pep
241	241	mmFAT11pep
301	301	hsFAT11pep
301	301	mmFAT11pep
361	361	hsFAT11pep
361	361	mmFAT11pep
421	421	hsFAT11pep
421	421	mmFAT11pep
481	481	hsFAT11pep
481	481	mmFAT11pep
541	541	hsFAT11pep
541	541	mmFAT11pep
601	601	hsFAT11pep
601	601	mmFAT11pep

Decoration 'Decoration #2': Shade (with solid bright yellow) residues that match the consensus named 'Consensus #1' exactly.

Figure 32

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Page 5

[illegible]

Decoration 'Decoration #1': Shades (with solid bright yellow) residues that match the consensus named 'Consensus #1' exactly.

Figure 33

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## hsFATP6

```

1      AAC GGC AAG CAA GCG CAA GGC AAT TAA TGT GAG TAG CTC ACT CAT TAG GCA CCG CAG GTC
61     TTA CAG TTT ACG CTT CCG GCG TCG TAT GTC GTG CGG AAT TGT GAG CCG ATA CCA ATT TCA
121    CAC AAG AAC CAG CCA TGA CAT GAT TAC GAA TTT AAT ACG ACT CAG TAT AGG GAA TTT GTC
181    CCT CGA GGC CAA GAA TTT GGC ACG AGG GGT GTC GAG CCG CCG GTC TTT TGG TGG GTA
241    GAG ACT GTA AAT CCG TGC GTC TCT CAG TGA TCA TCA TCC CAG CTT TTT CCG GTC CGA ATT
301    CAG CTT CCA ACT CAA GTC CCG GCG AAA GAG TAC CTG AGA GGA GAA AAG CTT CTG TCC CTG
361    GAC CTT CTT CTG AGG GCG GAG CTG GAG GTC CTT TGT TTT CCA GTC GCG CAG TGA CCG AAG
421    CTT AAT CTT CAG CAG CAG TGG GCG GAA CTT TTT CCG TGT AAA CTT ACG ATT CTG TTT CTT
481    AAG ATT CTT CCG CAT CTT GTC TCG CCG CCG AAA ACG TGA CAA GAA CTT CAG TGG TAA GTC
541    CTG AGT ACG GAG GAT CCG CCG TCT CCG TGG AGA GTC GTC CTT GTC AGA GGA GGA CCG TGG
601    TGG GGG CTG AGA TCA GAG CCG TCT TCT GGC CCA GTC GCG CCG TGT CTT CTG TCA TGG CTA
                                     M L L S M L
661    ACA GTC CCA GGG GTC GGA AAT GTC GTC CTG CAG TTT CTG CAG AAA CCG CTG TTT CTT TAC
721    T V L G A S N V V L H P L Q R L L F P Y
781    F V D D F M F V L K V V L I I I R L K K
Y E K R G E L V T V L D K F L S H A K R
841    CAA CTT CCG AAA CTT TTT ATC ATC TAT GAG GGA GAC ATC TAC ACC TAT CAG GAT GTA GAC
O P R K P F I I Y E G D I Y T Y Q D V D
901    AAA GGC AGC AGA GTC GTC CAT GTC TTT CTG AAG CAT TCT TCT CTG AAA AAG GTC GAC
K R S S R V A H V F L N H S S L K K G D
961    ACG GTC GTC CTG CCG ACG AAT GAG CCG GAT TCT GTC CAG GTC TGG TTT GTC CTT GTC
T V A L L H S N E P D F V H V W F G L A
1021   AAG CTT GTC GTC GTC GTC TTT CTT AAG ACC AAT CTT CCG TTT AAT TCT CTT CTT AAT
K L G C V V A F L N T N I A S H S L L N
1081   TGC AAT GTC GTC GTC GTC CCG AGA GTC CTA GTC GTC GTC GTC GTC GTC GTC GTC GTC GTC
C T R A C G P R A L V V G A D L L G T V
1141   GAA GAA ATT CTT CCA AGC TTT CCA GAA AAT AAT AGT GTC TGG GTC AAG GAT TCT GTC
E E I L P S L S E N I S V W G M K D S V
1201   CCA CAA GTC CTA ATT TCA CTT AAA GAA AAA CTG AGC ACC TCA CTT GAT GAG CCG GTC CCA
P Q G V I S L K E K L S T S P D E P V P
1261   CCG AGC CAG CAT GTC GTC TCA CTT CTT AAG TCT ACT TGT CTT TAC ATT TTT ACC TCT GGA
R S H H V V S L L K S T C L Y I P T S G
1321   ACA ACA GTC CTA CCA AAA GCA GTC GTC ATT AGC CAG GTC CAG GTC CTA AAG GTC TCT GTC
T T G L P K A A V I S Q L Q V L R G S A
1381   GTC CTG TGG GTC TTT GTC TGT ACT GTC CAT GAG ATT GTC CAT ACC CTT CTT CTG TAT
V L W A F G C T A H D I V Y I T L P L Y
1441   CAT AGT TCA GCA GTC ATC CTG GGA ATT CTT GGA TGT GTC GAG CTG GTC ACT TGT GTC
H S S A A I L G I S G C V E L G A T C V
1501   CTA AAG AAG AAA TTT TCA GCA AGC CAG TTT TGG AGT GAC TGT AAG AAT GAT GTC ACT
L K K K F S A S Q F W S D C K R Y D V T
1561   GTC TTT CAG TAT ATT GGA GAA CTT CTT TAC CTT TGC AAA CAA CTT AAG AGA GAA GAA
V P O Y I G E L C R Y L C K Q S K R E G
1621   GAA AAG GAT CAG AAG GTC CTT TGG CAA ATT GGA AAT GTC ATA CCG AGT GAT GTC TGG AGA
E K D H K V R L A I G N G I R S D V W A
1681   GAA TTT TCA GCA ATT GGA AAT ATA AAG GTC TGT GAA CTT TAT GCA GTC ACC GAA TCA
E F L D R P G N I K V C E L Y A A T E S
1741   AGC ATA CTT CTT ACG AAT TAC ACT GGG GGA ATT GGA CAA ATT GGG GGA ACA AAT CTG CTT
S I S F H N Y T G R I G A I G R T H L P
1801   TAC AAA CTT CTT TCT ACT TTT GAT CTA ACA AAG TAT GAT CTT CAG AAA GAT GAA CCG ATG
Y K L L S T P D L I K Y D F Q K D E P H
1861   AGA AAT GAG CAG GTC TGG TGT ATT CAT GTG AAA AAA GGA GAA CCG GGA CTT CTT ATT TCT
R N E Q G W C I H V K K G E P G L L I S
1921   CTA GTC AAT GCA AAA AAT CTT TCT TTT GTC TAT GTC GGG CTT TAT AAG CAG ACA AAA GAC
R V N A K N P F F G Y A G P Y K M T K D
1981   AAA CTG CTT TGT GAT GTC TTT AAG AAG GGA GAT GTC TAT AAT CTT GAT GAT TTA ACA
K L L C D V F K K G D V Y L N T G D L I
2041   GTC CAG GAT CAG GAT AAT TTT CTT TAT TTT TGG GAT CTT GGA GAT ACT TTT AAG CCG
V O D D Q D N F L Y F W D R T G D T F R W
2101   AAA GGA GAA AAT GTC GCA ACC ACT GAG GTC GTC GAT GTC ATT GGA ATG TGT GAT TCT ACA
K G E N V A T T E V A D V I G M L D F I
2161   CAG GAA GCA AAG GTC CAT GTC GTC GTC ATA TCA GTC TAT GAA GGA GGA GGA AAT GTC
Q E A N V Y G V A I S G Y E G R A G M A
2221   TCT ATT ATT TTA AAA CCA AAT ACA TCT CTA GAT TTT GAA AAA GTC TAT GAA CAA GTC GTC
S I I L K P N T S L D L E K V Y E Q V V
2281   ACA TTT CTA CCA GTC CAT GTC CTT CCA CCA CTT TTA AGA ATT CAG GAA AAA ATG GAA GCA
T P L P A Y A C P R F L R I Q E K H E A
2341   ACA GGA ACA TTT AAA CTA TGG AAG CAT CAG CTG GTC GGA GAT GTC ATT AAT CCA CTG AAA
T G T P K L L K H Q L V E D G F N P L K
2401   ATT TCT GAA CCA CTT TAC CCG ATG GAT AAT CTG AAA AAG CTT TAT GTC CTA CTG AAT GTC
S E P L Y F M D N L K K S Y V L L T R
2461   GAA CTT TAT GTC CAA ACA ATG TTA GGG GAA ATA CTT TAA GAT CTT TAT ACT TAG AAT
E L Y D Q I H L G E I K L
2521   TTT CAT ATG CTT TCT TAT GAA GAG CCA GAG GGG GTC AAT TGA TTT TTT AAT TTT GTC GGA
2581   AAG GTC CTT AAT ATT AAT TAT GCA TGT ACT ATA TTT CTT TAA TAT GAG GGA AAA TTT TTT
2641   AAT TGT AAT AAT ATT TAT TAT CTT TTT AAT TGA TAT AAA CAT TAG CTG ATT ATT CTT TTT
2701   AAT TAT CTG GAT AAT CAG TGT ATA ACT AAT TAT TTT CTT TAA TAT CAA GTC TTA AAT
2761   AAT AAT GTC GTC TAG CCG CTT GGA CAA TCA CTA AAA ATG TAT TTT CTA ACA GTC AAA ATT
2821   TCT AAT TTT GAA TAA AAG ATT AAA CTT TAT TGA AAA GAA AAA AAA AAA AAA CTG GTC
2881   GTC GTC

```

Figure 34

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Protein sequence 619 a.a. MLLSWLTVLGAG ... LYDQDLGGTKL

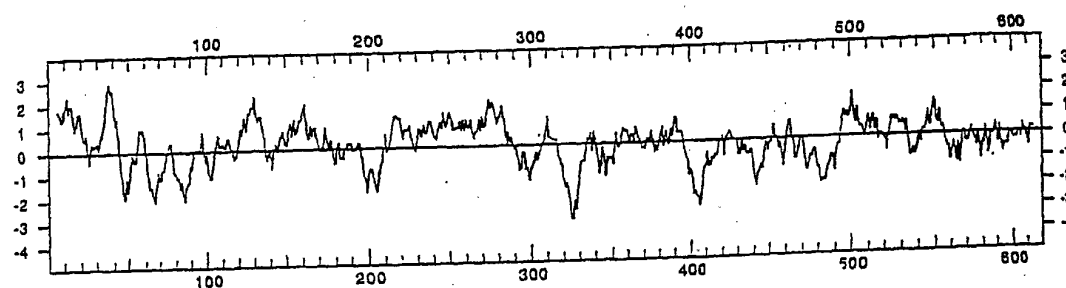


Figure 35A

Protein sequence 619 a.a. MLLSWLTVLGAG ... LYDQDLGGTKL

619 Amino Acids MW : 70056 Dalton

		n	n(%)	MW	MW(%)
A	ala	33	5.3	2344	3.3
C	cys	14	2.3	1442	2.1
D	asp	34	5.5	3910	5.6
E	glu	31	5.0	4000	5.7
F	phe	34	5.5	5000	7.1
G	gly	44	7.1	2508	3.6
H	his	15	2.4	1781	2.5
I	ile	37	6.0	4184	6.0
K	lys	48	7.8	6148	8.8
L	leu	75	12.1	8481	12.1
M	met	11	1.8	1461	2.1
N	asn	21	3.4	2394	3.4
P	pro	21	3.4	2038	2.9
Q	gln	18	2.9	2305	3.3
R	arg	27	4.4	4214	6.0
S	ser	40	6.5	3681	5.0
T	thr	30	4.8	3031	4.3
V	val	51	8.2	5052	7.2
W	trp	11	1.8	2046	2.9
X	unk	-	-	-	-
Y	tyr	26	4.2	4239	6.1
Z	---	-	-	-	-

Figure 35B



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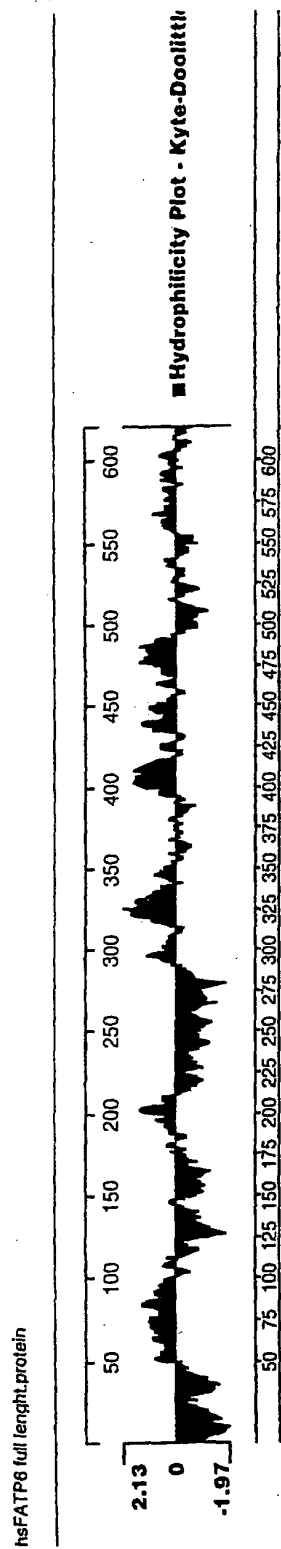


Figure 35C

Alignment Report of hFATP1,4,6 Alignment, using Clustal method with PAM250 residue weight table.

[illegible]

Decoration 'Decoration #1': Shade (with solid bright yellow) residues that match the Consensus exactly.

Figure 36

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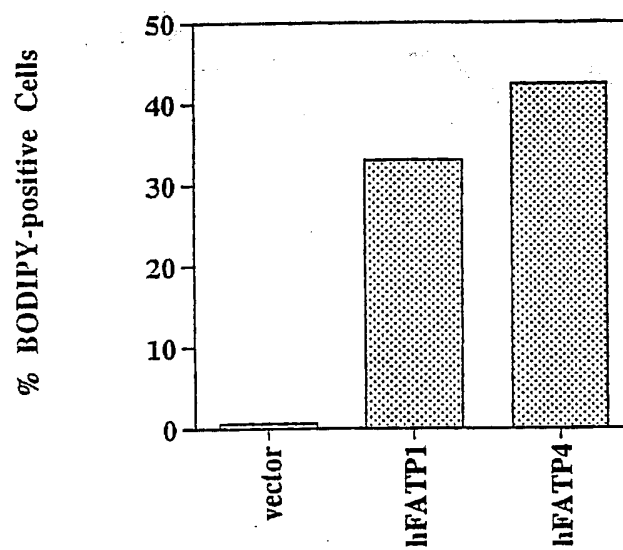
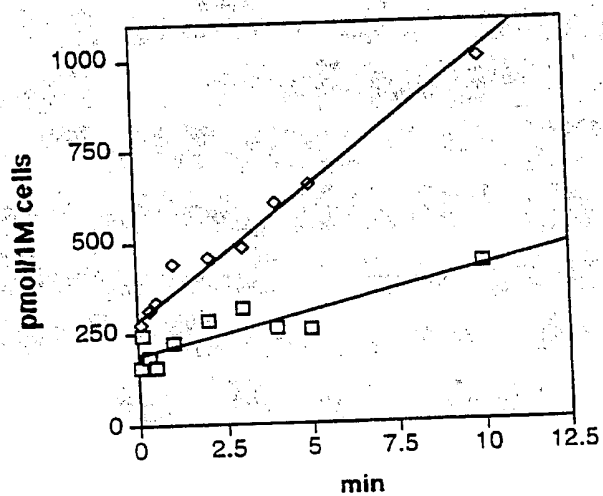


Figure 37

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□ 293 vector control: 23 pmol/(min\*1\*10<sup>6</sup> cells)  
◇ 293 FATP4 clone 7: 73 pmol/(min\*1\*10<sup>6</sup> cells)

Fig. 38

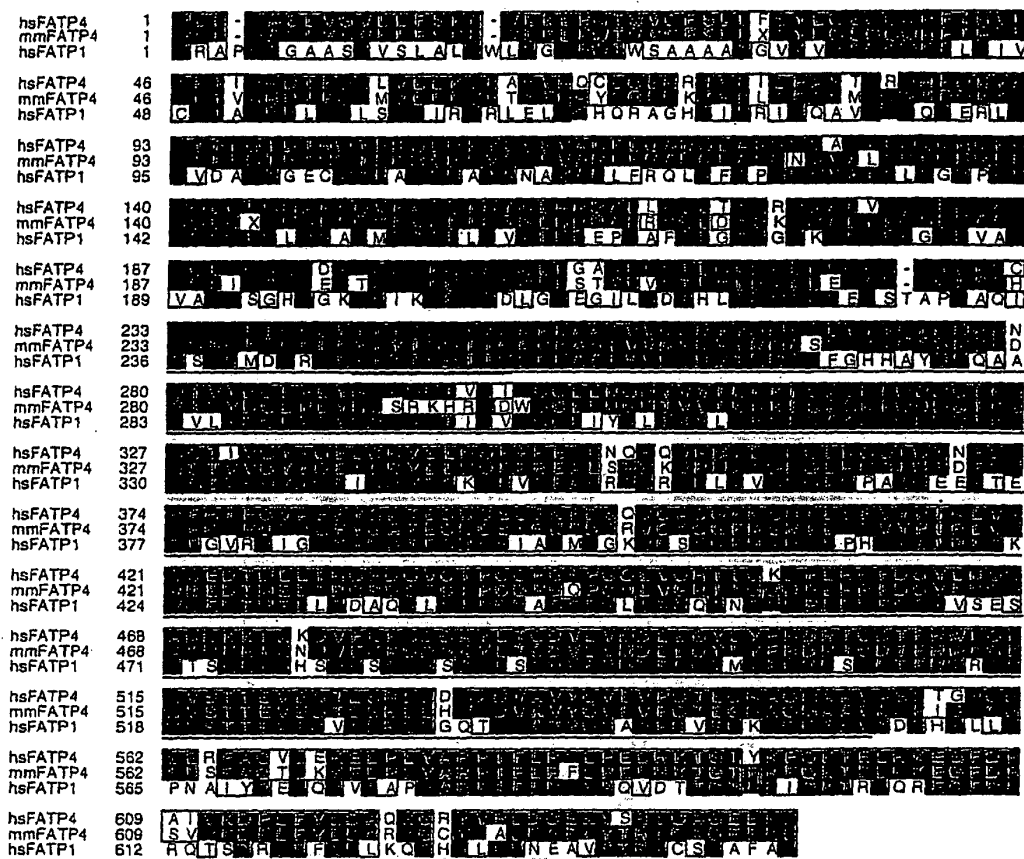


Fig. 39

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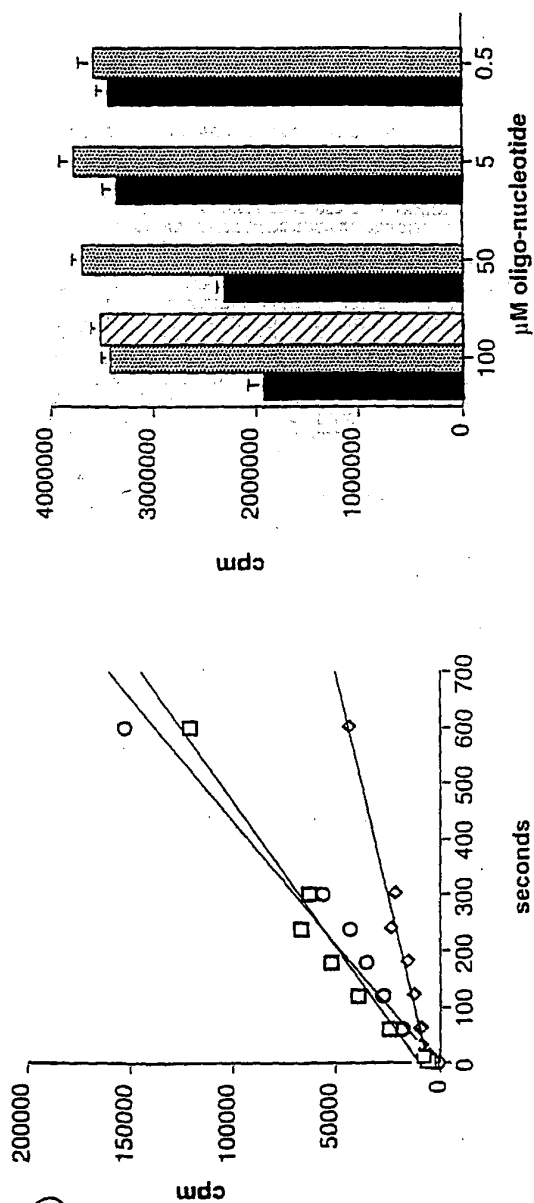


Fig. 40

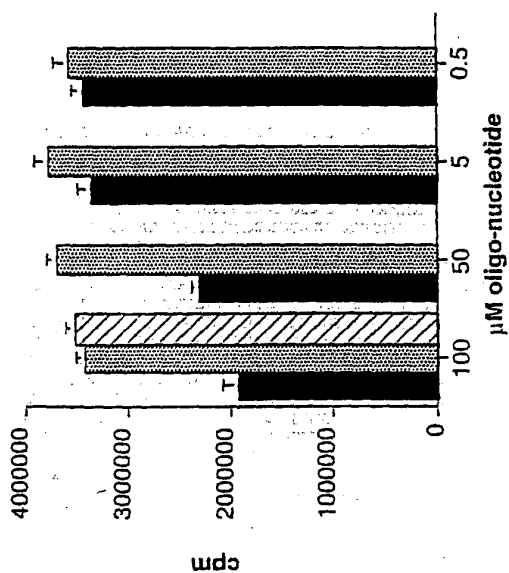


Fig. 41

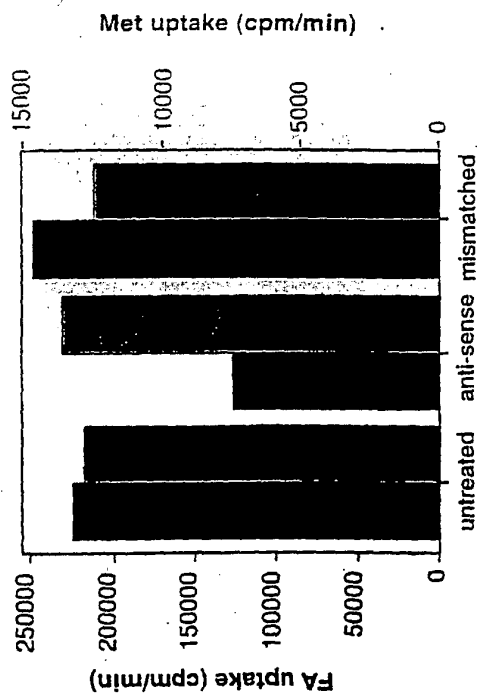


Fig. 42

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## mmFATP4 DNA sequence

ATGCTGCTTGGAGCCTCTCTGGTGGGGGCGCTACTGTTCTCCAAGCTAGTGTGAAGCTGCCCTGGAGCCAGGTGGGATT  
 CTCCTCTGTTGCTCCTGTACTTGGGGTCTGGTGGCTGGCGTTTCATCCGGGTCTTCATCAAGACGGTCAGGAGAGATATCT  
 TTGGTGGCATGGTCTCCTGAAGGTGAAGACCAAGGTGCGACGGTACCTTCAGGAGCGAGACGGTGCCTCTGCTGTTT  
 GCTTCAATGGTACAGCGCCACCCGGACAGACAGCCCTGATTTTCGAGGGCACAGACACTCACTGGACCTTCCGCCAGCT  
 GGATGAGTACTCCAGTAGTGTGGCCAACTTCCTGCAGGCCCGGGGCTTGGCTCAGGCAATGTAGTTGCCCTCTTTATGG  
 AAAACCGCAATGAGTTTGTGGTCTGTGGCTAGGCATGGCCAAAGCTGGGCGTGGAGGCGGCTCTCATCAACACCAACCTT  
 AGGCGGATGCCCTGCGCCACTGTCTTGACACCTCAAGGCCACGAGCTCTCATCTTTGGCAGTGAGATGGCCTCAGCTAT  
 CTGTGAGATCCATGCTAGCCTGGAGCCCACTCAGCCTCTTCTGCTCTGGATCCTGGGAGCCAGACAGTGGCCGCTCA  
 GCACAGAGCATCTGGACCTCTTCTGGAAGATGCCCGAAGCACCTGCCAGTCACTCAGACAAAGGGTTTACAGATAAG  
 CTCTTCTACATCTACACATCGGGCACCAACGGGGCTACCAAGCTGCCATTTGGTGTGCACAGCAGGTATTATCGTATGGC  
 TCTCCCTGGTGTACTATGGATTCCGCATGCCGCTGATGACATTTGTCTGACTGCCCTCCCTCTTACCACTCAAGCAGGA  
 AACATCGTGGGGATTGGCAGTGTCTTACTCCACGGCATGACTGTGGTGTATCCGGAAGAAGTTCTCAGCCTCCCGGTTCTGG  
 GATGATTTGATCAAGTACAACCTGCCAGTGGTACAGTACATTTGGCGAGCTCTGCCGTACTCTCTGAACAGCCACCCCG  
 TGAGGCTGAGTCTCGGCACAAGGTGCGCATGGCACTGGGCAACGGTCTCCGGCAGTCCATCTGGACCGACTTCTCCAGCC  
 GTTTCACATCCCCCAGGTGGCTGAGTTCTATGGGGCCACTGAATGCACTGTAGCCTGGGCAACTTTGACAGCCGGGTG  
 GGGGCTCTGTGGCTTCAATAGCCGCTCCTGCTTCTGTGATCCCTATCCGTTTGGTACGCTGTCAATGAGGATACCATGGA  
 ACTGATCCGGGGACCCGATGGAGTCTGCATTCCCTGTCAACAGGTGAGCCAGGCCAGCTGGTGGGTGCGATCATCCAGC  
 AGGACCTCTAGCCGCTTTCGACGGGTACCTCAACAGGGTGCCAAACAAGAAGATTGCTAATGATGTCTTCAAGAAG  
 GGGGACCAAGCCTACCTCACTGGTGACCTCTGGTGTGATGATGAGTGGGTTACCTGTACTTCCGAGATCGCACTGGGGA  
 CACGTTCCGCTGGAAAGGGGAGAATGTATCTACCACTGAGGTGGAGGGGCACACTCAGCCGCTGCTTCATATGGCAGATG  
 TGGCAGTTTATGGTGTGAGGTGCCAGGAAGTGAAGGCCGAGCAGGAATGGCTGCCGTTGCAAGTCCCATCAGCAACTGT  
 GACCTGGAGAGCTTTGCACAGACCTTGAAGAGGAGCTGCTCTGTATGCCCCCCCCATCTTCTGCGCTTCTTGCCTGA  
 GCTGCAACAAGACAGGACCTTCAAGTTCAGAGAAGCAGAGTTGCGGAAGGAGGGCTTGAACCATCTGTTGTGAAGAC  
 AGTGAATCACTGCGCTTCCCGACCTCCAGAGGCTTCTGTGAAAGTCTCATCCAGCTGTGTCTTCTGGTCCAGGGC  
 TGGCCCTTGGCCAGGGTTCTGATAGGCTCCTTTAGGATGGTATCTTGGGTCAGCGGGCCAGGGTGTGGGAGAGGAG  
 TCACTAAGATCCCTCAATCAGAAGGGAGCTTACAAAGGAACCAAGGCAAGCTGTAGACTCAGGAAGCTAAGTGTGAG  
 GAGACTATAGTGGCCAGTCACTCCATGTCCACAGAGGATCTTGGTCCAGAGCTGCCAAAGTGTACCTCTCCCTGCTGC

ACCTCTGGGGAAAAGAGGACAGCATGTGGCCACTGGGCACTGTCTCAAGAAGTCAGGATCACACACTCAGTCCTGTTT  
 CTCAGGTTCCCTGTTCTTGTCTCGGGAGGGAGGGACGAGTGTCTGTCTCTCTGCTCTGCTGCTGTGAGTCTGTG  
 TTGCTTCTCCATCTGCTCCTAGCCTGAGTGTGGGTGGAACAGGCATGAGGAGAGTGTGGCTCAGGGGCCAATAACTCTGC  
 CTTGACTCCTCTTAAA

Figure 43A

## mmFATP4 protein sequence

MLLGASLVGALLFSKLVLKLPWTQVGSLLLLYLGSQGWRFIRVFIKTVRRDIFGGMVLLKVTKVRRYLQERKTVPLLF  
 ASMVQRHDPKLTALIFEGTDTHWTFRLDEYSSSVANFLQARGLASGNVVALFMENRNEFVGLWLGMAKLGVRAALINTNL  
 RRDALRHCLDTSKARALIFGSEMAISCEIHASLEPTLSLFCSGSWEPTVFPVSTEHLDPLLEDAPKHLPSHPDKGFTDK  
 LFYITTSGTGLPKAAIVVHSRYRMAASLVVYGFMRPDDIVYDCLPLYHSSRKHGRDQCLLHGMTVVIKXFSASRFFW  
 DDCKYKNTVQYIGELCRYLLNQPPREAESRHKVRMALGNLRQSIWTFSSRFHIPQVAEFYGATECNCSLGNFDSRV  
 GACGFNSRILSFVYPIRLVVRNEDTMELIRGPDGVCIPCPGPGQVLGRIIQODPLRRFDGYLNOGANNKKIANDVFKK  
 GDQAYLTDGVLVMDLGYLYFRDRDGTFRWKGENVSTTEVEGTLRLLHMDVAVYGVVPGTEGRAGMAAVASPI SMC  
 DLESFAOTLKKELPLYARPIFLRFLPELHKGTGTFKFKTELKKEGDFPSVVKDPLFYLDARKGCYVALDQEA YTRIQA  
 EKL

Figure 43B

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hsFATP1 full lenght.DNA

10 20 30 40  
TCGACCCACGGCGTCCGGGACCCCAAAGCAGAAGCCCGCA 40  
CAGTAGGCACAGCGCACCCAAGAAGGGTCCAGGAGTCTGC 80  
AGAAACAGAAAGGTCCCCGGCCTCAGCCTCCTAGTCCCTG 120  
CCTGCCTCCTGCCTGAGCTTCTGGGAGACTGAAGGCACGG 160  
CTTGACAGCTTCAGGATGCGGGCTCCGGGTGCGGGCGCGGC 200  
210 220 230 240  
CTCGGTGGTCTCGCTGGCGCTGTTGTGGCTGCTGGGGCTG 240  
CCGTGGACCTGGAGCGCGGCAGCGGCGCTCGGCGTGTACG 280  
TGGGCAGCGGGCGGCTGGCGCTTCTGCGCATCGTCTGCAA 320  
GACCGCGAGGCGAGACCTCTTCGGTCTCTGTGCTGATC 360  
CGCGTGCGCCTGGAGCTGCGGGCGGCACAGCGTGCCGGCC 400  
410 420 430 440  
ACACCATCCCGCGCATCTTTCAGGCGGTAGTGACGCGACA 440  
GCCCGAGCGCCTGGCGCTGGTGGATGCCGGGACCGCGAG 480  
TGCTGGACCTTTGCGCAGCTGGACGCCTACTCCAATGCGG 520  
TAGCCAACCTCTTCGGCCAGCTGGGCTTCGCGCCGGGCGA 560  
CGTGGTGGCCATCTTCTGAGGGCGCGCCGAGTTCTGTG 600  
610 620 630 640  
GGGCTGTGGCTGGGCCTGGCCAAGGCGGGCATGGAGGCCG 640  
CGCTGCTCAACGTGAACCTGCGGCGGAGCCCCCTGGCCTT 680  
CTGCCTGGGCACCTCGGGCGCTAAGGCCCTGATCTTTGGA 720  
GGAGAAATGGTGGCGGCGGTGEGCCGAAGTGAGCGGGCATC 760  
TGGGGAAAAGTTTGATCAAGTTCTGCTCTGGAGACTTGGG 800  
810 820 830 840  
GCCCCAGGGCATCTTGCCGGACACCCACCTCCTGGACCCG 840  
CTGCTGAAGGAGGCCTCTACTGCCCCCTTGGCACAGATCC 880  
CCAGCAAGGGCATGGACGATCGTCTTTTCTACATCTACAC 920  
GTCGGGGACCAACGGGCTGCCCCAAGGCTGCCATTGTCTG 960  
CACAGCAGGTACTACCGCATGGCAGCCTTCGGCCACCACG 1000  
1010 1020 1030 1040  
CCTACCGCATGCAGGCGGCTGACGTGCTCTATGACTGCCT 1040  
GCCCCGTGACCACTCGGCAGGAAACATCATCGGCGTGGGG 1080  
CAGTGTCTCATCTATGGGCTGACAGTCGTCTCCGCAAGA 1120  
AATTCTCGGCCAGCCGCTTCTGGGACGACTGCATCAAGTA 1160  
CAACTGCACGGTGGTTCAGTACATCGGGGAGATCTGCCGC 1200

Fig. 44A



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## hsFATP1 full lenght.DNA

```
1210      1220      1230      1240
TACCTGCTGAAGCAGCCGGTGC GCGAGGCGGAGAGGCGAC 1240
ACCGCGTGCGCCTGGCGGTGGGGAACGGGCTGCGTCCTGC 1280
CATCTGGGAGGAGTTACGGAGCGCTTTCGGCGTACGCCAA 1320
ATCGGGGAGTTCTACGGCGCCACCGAGTGAACCTGCAGCA 1360
TTGCCAACATGGACGGCAAGGTCGGCTCCTGTGGTTTCAA 1400

1410      1420      1430      1440
CAGCCGCATCCTGCCCCACGTGTACCCCATCCGGCTGGTG 1440
AAGGTCAATGAGGACACAATGGAGCTGTGCGGGATGCCC 1480
AGGGCCTCTGCATCCCCTGCCAGGCCGGGAGCCTGGCCT 1520
CCTTGTGGGTGAGATCAACCAACAGGACCCGCTGCGCCGC 1560
TTCGATGGCTATGTGAGCGAGAGCGCCACCAGCAAGAAGA 1600

1610      1620      1630      1640
TCGCCCACAGCGTCTTCAGCAAGGGCGACAGCGCCTACCT 1640
CTCAGGTGACGTGCTAGTGATGGATGAGCTGGGCTACATG 1680
TACTTCCGGGACCGTAGCGGGGACACCTTCCGCTGGCGAG 1720
GGGAGAACGTCTCCACCACCGAGGTGGAGGGCGTGCTGAG 1760
CCGCCTGCTGGGCCAGACAGACGTGGCCGCTCTATGGGGTG 1800

1810      1820      1830      1840
GCTGTTCCAGGAGTGGAGGGTAAGGCAGGGATGGCGGCCG 1840
TCGCAGACCCCCACAGCCTGCTGGACCCCAACGCGATATA 1880
CCAGGAGCTGCAGAAGGTGCTGGCACCCCTATGCCCGGCC 1920
ATCTTCTGCGCCTCCTGCCCCAGGTGGACACCACAGGCA 1960
CCTTCAAGATCCAGAAGACGAGGCTGCAGCGAGAGGGCTT 2000

2010      2020      2030      2040
TGACCCACGCCAGACCTCAGACCGGCTCTTCTTCTCTGGAC 2040
CTGAAGCAGGGCCACTACCTGCCCTTAAATGAGGCAGTCT 2080
ACACTCGCATCTGCTCGGGCGCCTTCGCCCTCTGAAGCTG 2120
TTCCTCTACTGGCCACAACTCTGGGCCTGGTGGGAGAGG 2160
CCAGCTTGAGCCAGACAGCGCTGCCACAGGGGTGGCCGCCT 2200

2210      2220      2230      2240
AGTACACACCCACCTGGCCGAGCTGTACCTGGCACGGCCC 2240
ATCCTGGACTGAGAACTGGAACCTCAGAGGAACCCGTGC 2280
CTCTCTGCTGCCTTGGTGGCCCTGTGTCTGCCTCCTCTCC 2320
CTGCTTTTCAGCCTCTGTCTCCTTCCATCCCTGTCCCTGT 2360
CTGGCCTTAACCTCTTCCCTCTCTTTCTTTCTTTCTTTCT 2400

2410      2420      2430      2440
TTCTTTTTTTTTTAAGATAGAGTCTCACTCTGCTGCCCGGG 2440
CTAGAGTGCAGTGGTGGGATCTCGGCTCACTGCAACCTCT 2480
GCCTCCTGGGGTTCAAGTGATCCTCCACCTCAGCCTCCT 2520
GAGTAGCTGGGATTACAGGCACCCGCCACCACGTCCAGCT 2560
AATTTTTATATTTTATAGAGACGGGGTTTCACCATGTT 2600
```

Fig. 44B

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## hsFATP1 full length.DNA

```
      2610      2620      2630      2640
      | | | | | | | | | | | | | | | | | |
GGTCAGGCTGGTCTTGAACCTCTGACCTCAGGTGATCCGC 2640
TGGCCTCGGCCTCCAGAGTGCTGGGATTATAGGCGTGAG 2680
CCTCTGCCCCGGCCTTTCTTTTTCTCTCCTCTCCTGCC 2720
GAGAGTGGAACACACGTGTCCTGGGAGCTGCATCTTGTGT 2760
AGGGTCCAGCTGCTTTTGGGGACTGCAGGAATCATCTCCC 2800
      2810      2820      2830      2840
      | | | | | | | | | | | | | | | | | |
CTGGGCCCTGGACTCGGACTGGGGCCTCCCCACCTCCCTC 2840
TCGGCTGTGCCTTACGGAGCCCCAATCCAGGCCTCCTGTG 2880
GCTGTTGGGTTCCAGATGCTGCAGCTCCATGTGACTTCCA 2920
AGCAGGCCCTCCGCCCTCCCTGCTGAATGGAGGAGCCGGG 2960
GGTCCCCCAGGCCAACTGGAAAATCTCCAGGCTAGGCCA 3000
      3010      3020      3030      3040
      | | | | | | | | | | | | | | | | | |
ATTGCCTTTTGCACTTCCCCGTTCTGTGCATTTCCCCA 3040
GCCCCACCTTCCCCCTCCTGATGCCCTGAAAGCTTCCGGAA 3080
TTGACTGTGACCACTTGGATGTCACCACTGTCAGCCCCCTG 3120
CCTTGATGTCCCCATTTAGCCATCTCCATGGAGCTCCTGC 3160
TGGAGGGGCCCTGAACCTGCACTGCGTGGCTGCCAGCCA 3200
      3210      3220      3230      3240
      | | | | | | | | | | | | | | | | | |
GCTGCCTCCTGTCTGGGAGGAGGCCTCCTGGGTGTCTCTC 3240
ATCTGGTGTGTCTACTGGAGGGTCCCACAGGAGAGGCAGC 3280
AGAGGGGTGAGGGGAGGTCTCTGCGGGGGGTGGCCTCT 3320
CAAGCCTCAGGGGTCTAGCCTGTTGAATATACCCACCT 3360
GGTGGGTGGCCCCCTCCGATGTCCCCACTGATGGCTCTGAC 3400
      3410      3420      3430      3440
      | | | | | | | | | | | | | | | | | |
ACCGTGTGGTGGCGATGTCCCAGACAATCCCACCAGGAC 3440
GGCCCAGACATCCCTACTGGCTTCGCTGGTGGCTCATCTC 3480
GAACATCCACGCCAGCCTTTCTGGGGCCGGCCACCCAGGC 3520
CGCCTGTCCGTCTGTCTCCCTCCAGCAGCACCCCTGGC 3560
CCCTGGAGTGGTGGGGCCATGGCAAGAGACACCGTGGCGT 3600
      3610      3620      3630      3640
      | | | | | | | | | | | | | | | | | |
CTCATGTGAACCTTTCTGGGCACTGTGGTTTTTTTCTTA 3640
ATTGATTTAAGAAATAAACCTGAAGACCGTCTGGTGAAAA 3680
AAAAAAAAAAAAA 3694
```

Fig. 44C

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hsFATP1 full lenght.protein

10 20 30 40  
MRAPGAGAASVVSLALLWLLGLPWTWSAAAAAGVYVGSGG 40  
WRFLRIVCKTARRDLFGLSVLIRVRLELRRHORAGHTIPR 80  
IFOAVVQROPERLALVDAGTGECWTFAQLDAYSNAVANLF 120  
ROLGFAPGOVVAIFLEGRPEFVGLWLGLAKAGMEAALLNV 160  
NLRREPLAFCLGTSGAKALIFGGEMVAAVAIEVSGHLGKSL 200  
210 220 230 240  
IKFCSGDLGPEGILPOTHLLDPLLKEASTAPLAQIPSKGM 240  
DDRIFYIYTSGETTGLPKAAIVVHSRYRMAAFGHHAYRMO 280  
AADVLYDCLPLYHSAGNIIGVGQCLIIYGLTVVLRKKFSAS 320  
RFWDDCIKYNCTVVOYIGEICRYLLKQPVREAERRHRVRL 360  
AVGNGLRPAIWEEFTERFGVRQIGEFYGATECNCSIANMD 400  
410 420 430 440  
GKVGSCGFNSRIILPHYYPIRLVKVNEDTMELLRDAQGLCI 440  
PCQAGEPGLLVGQINQODPLRRFDGYVSESATSKKIAHSV 480  
FSKGDSAYLSGDVLMDELGYMYFRDRSGDTRWRGENVS 520  
TTEVEGYLSRLLGQTDVAVYGVAVPGVEGKAGMAAVADPH 560  
SLLDPNAIYQELQKVLAPYARPIFLRLLPQVDTTGTFTKIQ 600  
610 620 630 640  
KTRLQREGFDPROTSDRLLFFLDLKQGHYLPNEAVYTRIC 640  
SGAFAL. 647

Fig. 45

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hsVLACS full lenght.DNA

```

      10      20      30      40
      |      |      |      |
GGAATTCCAAAAAAAAAAAAATACGACTACACCTGCTCCGG 40
AGCCCGCGGCGGTACCTGCAGCGGAGGAGCTCTGTCTTCC 80
CCTTCACTCTACGCGAGCCCGGCGTCCC GCCGCGTGCGCC 120
CCGGCGCAGCCCGCCAGTCCGCCCGGAGCCCGCCAGTCG 160
CCGCGCTGCACGCCCGGGGTGAACCTCTGCCCTCGCTGG 200
      210      220      230      240
      |      |      |      |
GACAGAGGGCCCCCGCAGCCGTCATGCTTTCCGCCATCTAC 240
ACAGTCTTGGCGGGACTGCTGTTCTGCGCTCCTGGTGA 280
ACCTCTGCTGCCCCATACTTCTTCCAGGACATAGGCTACTT 320
CTTGAAGGTGGCCCGCGTGGGCCGGAGGGTGC GCAGCTAC 360
GGGCAGCGGCGGCCGCGCGCACCATCCTGCGGGCGTTCC 400
      410      420      430      440
      |      |      |      |
TGGAGAAAGCGCGCCAGACGCCACACAAGCCTTTTCTGCT 440
CTTCCGCGACGAGACTCTCACCTACGCGCAGGTGGACCGG 480
CGCAGCAATCAAGTGGCCCGGGCGCTGCACGACCACCTCG 520
GCCTGCGCCAGGGAGACTGCGTGGCGCTCCTTATGGGTA 560
CGAGCCGGCCCTACGTGTGGCTGTGGCTGGGGCTGGTGAAG 600
      610      620      630      640
      |      |      |      |
CTGGGCTGTGCCATGGCGTGCCTCAATTACAACATCCGCG 640
CGAAGTCCCTGCTGCACTGCTTCCAGTGCTGCGGGGCGAA 680
GGTGCTGCTGGTGTGCCAGAACTACAAGCAGCTGTGCGAA 720
GAGATACTGCCAAGCCTTAAAAAAGATGATGTGTCCATCT 760
ATTATGTGAGCAGAAGCTTCTAACACAGATGGGATTGACTC 800
      810      820      830      840
      |      |      |      |
TTTCTGGACAAAGTGGATGAAGTATCAACTGAACCTATC 840
CCAGAGTCATGGAGGTCTGAAGTCACTTTTCCACTCCTG 880
CCTTATACATTTATACTTCTGGAACCAAGGCTTTCCAAA 920
AGCAGCCATGATCACTCATCAGCGCATATGGTATGGAAGT 960
GGCCTCACTTTTGTAAGCGGATTGAAGGCAGATGATGTCA 1000
      1010      1020      1030      1040
      |      |      |      |
TCTATATCACTCTGCCCTTTTACCACAGTGCTGCACTACT 1040
GATTGGCATTTCACGGATGATTGTGGCTGGTGTCTACTCTT 1080
GCCTTGGGACTAAATTTTCAGCCAGCCAGTTTGGGATG 1120
ACTGCAGAAAATACAACGTCAGTGTCAATTCAGTATATCGG 1160
TGAAGTGTCTCGGTATTTATGCAACTCACCACAGAAACCA 1200

```

Fig. 46 A

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hsVLACS full lenght.DNA

1210	1220	1230	1240
AATGACCGTGATCATAAAGTGAGACTGGCACTGGGAAATG 1240			
GCTTACGAGGAGATGTGTGGAGACAATTTGTCAAGAGATT 1280			
TGGGGACATATGCATCTATGAGTTCTATGCTGCCACTGAA 1320			
GGCAATATTGGATTTATGAATTATGCGAGAAAAAGTTGGTG 1360			
CTGTTGGAAGAGTAACTACCTACAGAAAAAATCATAAC 1400			
1410	1420	1430	1440
TTATGACCTGATTAAATATGATGTGGAGAAAGATGAACCT 1440			
GTCCGAGATGAAAATGGATATTGCGTCAGAGTTCCCAAAG 1480			
GTGAAGTTGGACTTCTGGTTTGCAAAATCACACAACCTTAC 1520			
ACCATTTAATGGCTATGCTGGAGCAAAGGCTCAGACAGAG 1560			
AAGAAAAAAGTGAAGATGTCTTAAGAAAGGAGACCTCT 1600			
1610	1620	1630	1640
ATTTCAACAGTGGAGATCTCTTAATGGTTGACCATGAAAA 1640			
TTTCATCTATTTCCACGACAGAGTTGGAGATACATTCCGG 1680			
TGGAAAGGGGAAAAATGTGGCCACCACTGAAGTTGCTGATA 1720			
CAGTTGGACTGGTTGATTTGTCCAAGAAGTAAATGTTTA 1760			
TGGAGTGCATGTGCCAGATCATGAGGGTCGCATTGGCATG 1800			
1810	1820	1830	1840
GCCTCCATCAAAATGAAAGAAAACCATGAATTTGATGGAA 1840			
AGAAACTCTTTTCAGCACATTGCTGATTACCTACCTAGTTA 1880			
TGCAAGGCCCGGTTTCTAAGAATACAGGACACCATTGAG 1920			
ATCACTGGAACTTTTAAACACCGCAAAATGACCCTGGTGG 1960			
AGGAGGGCTTTAACCTGCTGTCAATCAAGATGCCTTGTA 2000			
2010	2020	2030	2040
TTTCTTGATGACACAGCAAAAATGTATGTGCCTATGACT 2040			
GAGSACATCTATAATGCCATAAGTGCTAAAACCTGAAAC 2080			
TCTGAATATTCCCAGGAGGATAACTCAACATTTCCAGAAA 2120			
GAAACTGAATGGACAGCCACTTGATATAATCCAACCTTAA 2160			
TTTGATTGAAGATTGTGAGGAAATTTGTAGGAAATTTGC 2200			
2210	2220	2230	2240
ATACCCGTAAAGGGAGACTTTTTTAAATAACAGTTGAGTC 2240			
TTTGCAAGTAAAAAGATTTAGAGATTATTATTTTTCAGTG 2280			
TGCACCTACTGTTTGTATTTGCAAACTGAGCTTGTTGGAG 2320			
GGAAGGCATTATTTTTTAAATACTTAGTAAATTAAATGA 2360			
AC 2362			

Fig. 46B

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hsVLACS full lenght.protein

10 20 30 40  
MLSAIYTVLAGLLFLPLLVLNCCPYFFQDIGYFLKVAAVG 40  
RRVRSYGORRPARTILRAFLEKARQTPHKPFLLFRDETLT 80  
YAQVDRRSNQVARALHDHLGLRQGDVALLMGNEPAYVWL 120  
WLGLVKLGCAMACLNYNIRAKSLLHCFQCCGAKVLLYSPE 160  
LQAAVEEILPSLKKDDVSIIYVSRSTSNTDGIDSFLDKVDE 200  
210 220 230 240  
VSTEPESWRSEVTFSTPALYIYTSGETGLPKAAMITHQ 240  
RIWYGTGLTFVSGLKADDVIYITLPHYHSAALLIGIHGCI 280  
VAGATLALRTKFSASQFWDDCRKYNVTVIOYIGELLRYLC 320  
NSPQKPNDRDHKVRRLALGNGLRGDVWRQFVKRFGDICIYE 360  
FYAATEGNIGFMNYARKVGAVGRVNYLOKKIITYDLIKYD 400  
410 420 430 440  
VEKDEPVRDENGVCVRVPKGEVGLLVCKITQLTPFNGYAG 440  
AKAQTEKKLRDVFKKGDLYFNSGDLLMVDHENFIYFHDR 480  
VGDTFRWKGENVATTEVADTVGLVDFVQEVNVYGVHVPDH 520  
EGRIGMASIKMKENHEFDGKKLFQHIADYLPSYARPRFLR 560  
IQOTIEITGTFKHKRMTLVEEGFNPAVIKDALYFLODTAK 600  
610 620 630 640  
MYVPMTEDIYNAISAKTLKL. 621

Fig. 47

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hsFATP3 partial.DNA

```

      10      20      30      40
      +-----+
AAGTTCTCGGCTGGTCAGTTCTGGGAAGATTGCCAGCAGC 40
ACAGGGTGACGGTGTTCCAGTACATTGGGGAGCTGTGCCG 80
ATACCTTGTC AACCAGCCCCGAGCAAGGCAGAACGTGGC 120
CATAAGGTCCGGCTGGCAGTGGGCAGCGGGCTGCGCCAG 160
ATACCTGGGAGCGTTTTGTGCGGCGCTTCGGGCCCCTGCA 200
      210      220      230      240
      +-----+
GGTGTGAGACATATGGACTGACAGAGGGCAACGTGGCC 240
ACCATCAACTACACAGGACAGCGGGGCGCTGTGGGCGTG 280
CTTCCTGGCTTTACAAGCATATCTTCCCTTCTCCTTGAT 320
TCGCTATGATGTCACCAAGGAGAGCCAATTCGGGACCCC 360
CAGGGGCACTGTATGGCCACATCTCCAGGTGAGCCAGGGC 400
      410      420      430      440
      +-----+
TGCTGGTGGCCCCGGTAAGCCAGCAGTCCCCATTCTGGG 440
CTATGCTGGCGGGCCAGAGCTGGCCAGGGGAAGTTGCTA 480
AAGGATGTCTTCCGGCCTGGGGATGTTTTCTTCAACTG 520
GGGACCTGCTGGTCTGCGATGACCAAGGTTTTCTCGCTT 560
CCATGATCGTACTGGAGACACCTTCAGGTGGAAGGGGAG 600
      610      620      630      640
      +-----+
AATGTGGCCACAACCGAGGTGGCAGAGGTCTTCGAGGCC 640
TAGATTTTCTTCAGGAGGTGAACGTCTATGGAGTCACTGT 680
GCCAGGGCATGAAGGCAGGGCTGGAATGGCAGCCCTAGTT 720
CTGCGTCCCCCCCCACGCTTTGGACCTTATGCAGCTCTACA 760
CCCACGTGCTGAGAACTTGCCACCTTATGCCCGGCCCCG 800
      810      820      830      840
      +-----+
ATTCCTCAGGCTCCAGGAGTCTTTGGCCACCACAGAGACC 840
TTCAAACAGCAGAAAGTTCGGATGGCAAATGAGGGCTTCG 880
ACCCACAGCACCCTGTCTGACCCACTGTACGTTCTGGACCA 920
GGCTGTAGGTGCCTACCTGCCCCCTCACAAC TGCCGGTAC 960
AGCGCCCTCCTGGCAGGAAACCTTCGAATCTGAGAACTTC 1000
      1010      1020      1030      1040
      +-----+
CACACCTGAGGCACCTGAGAGAGGAACTCTGTGGGGTGGG 1040
GGCCGTGTCAGGTGTACTGGGCTGTGAGGGATCTTTTCTA 1080
TACCAGAACTGCGGTCACTATTTTGTAAATAAATGTGGCTG 1120
GAGCTGATCCAGCTGTCTCTGACAAAAA AAAAAAAAAA 1160
AAAGGGCGGCCGC 1173

```

Fig. 48

hsFATP3partial.protein

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10 20 30 40  
KFSAGQFWEDCQQHRVTVFYIGELCRYLVNQPPSKAERG 40  
HKVRLAVGSGLRPDWTFVRRFGPLQVLETYGLTEGNVA 80  
TINYTGORGAVGRASWLYKHIFPFLIRYDVTGTGEPIRDP 120  
QGHCMATSPGEPGLLVAPVSQQSPFLGYAGGPFLAQGKLL 160  
KDVFRPGDVFFNTGDLLVCDDQGFLRFHRTGDTFRWKGE 200  
210 220 230 240  
NVATTEVAEVFEALDFLOEVNVYGVTVPGHEGRAGMAALV 240  
LRPPHALDLMQLYTHVSENLPYARPRFLRLQESLATTET 280  
FKQQKVRMANEGFDPSTLSDPLYVLDQAVGAYLPLTTARY 320  
SALLAGNLR. 331

Fig. 49



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hsFATP4 full length

```
      10      20      30      40
CGACCCACGCGTCCGGGCGGGCGGGGCCGGGCGGCGGGCG 40
GGGCTGGCGGGGCGGGCGGGCCATGCAGGGCGCAGAGCCG 80
GCTAAACCCCTGCTGAGACCCGGCTCCGTGCGTCCAGGGGC 120
GGCTAATGCCCTCACGCTGTCTACGCTGCTGCAACCGGG 160
CCGCATCTGGACGGGCGCGCGCGGGAGCCGACGCCG 200
      210      220      230      240
GGCCACAATGCTGCTTGGAGCCTCTCTGGTGGGGGTGCTG 240
CTGTTCTCCAAGCTGGTGCTGAAACTGCCCTGGACCCAGG 280
TGGGATTCTCCCTGTTGTTCTCTACTTGGGATCTGGCGG 320
CTGGCGCTTCATCCGGGCTTTCATCAAGACCATCAGGCGC 360
GATATCTTTGGCGGCTGGTCTCTCTGAAGGTGAAGGCAA 400
      410      420      430      440
AGGTGCGACAGTGCCTGCAGGAGCGGCGGACAGTGCCCAT 440
TTTGTTCCTCTACCGTTTCGGCGCCACCCCGACAAGACG 480
GCCCTGATCTTCGAGGGCACAGATACCCACTGGACCTTCC 520
GCCAGCTGGATGAGTACTCAAGCAGTGTAAGCAACTTCCT 560
GCAGGCCCCGGGCGCTGGCTTCGGGCGATGTGGCTGCCATC 600
      610      620      630      640
TTCATGGAGAACCACAATGAGTTTCGTGGGCTATGGCTGG 640
GCATGGCCAAGCTCGGTGTGGAGGCAGCCCTCATCAACAC 680
CAACCTGCGGCGGGATGCTCTGCTCCACTGCCTCACCACC 720
TCGCGCGCACGGGCCCTTGCTTTGGCAGCGAAATGGCCT 760
CAGCCATCTGTGAGGTCCATGCCAGCCTGGACCCCTCGCT 800
      810      820      830      840
CAGCCTCTTGCTCTGGCTCCTGGGAGCCCGGTGCGGTG 840
CCTCCAAGCACAGAACACCTGGACCCCTCTGCTGAAAGATG 880
CTCCCAAGCACCTTCCAGTTGCCCTGACAAGGGCTTCAC 920
AGATAAACTGTTCTACATCTACACATCCGGCACCACAGGG 960
CTGCCCAAGGCCGCCATCGTGGTGACAGCAGGTATTACC 1000
      1010      1020      1030      1040
GCATGGCTGCCCTGGTGTACTATGGATTCCGCATGCGGCC 1040
CAACGACATCGTCTATGACTGCCTCCCCCTCTACCACTCA 1080
GCAGGAAACATCGTGGGAATCGGCCAGTGCCTGCTGCATG 1120
GCATGACGGTGGTGATTTCGGAAGAAGTTCTCAGCCTCCCG 1160
GTTCTGGGACGATTGTATCAAGTACAAGTGCACGATTGTG 1200
```

Fig. 50A

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hsFATP4 full length

```
1210      1220      1230      1240
.....
CAGTACATTGGTGAACGTGTGCCGCTACCTCCTGAACCAGC 1240
CACC GCGGGAGGCAGAAAACCAGCACCAGGTTGCGATGGC 1280
ACTAGGCAATGGCCTCCGGCAGTCCATCTGGACCAACTTT 1320
TCCAGCCGCTTCCACATACCCAGGTGGCTGAGTTCTACG 1360
GGGCCACAGAGTGCAACTGTAGCCTGGGCAACTTCGACAG 1400

1410      1420      1430      1440
.....
CCAGGTGGGGGCTGTGGTTTCAATAGCCGCATCCTGTCC 1440
TTCGTGTACCCCATCCGGTTGGTACGTGTCAACGAGGACA 1480
CCATGGAGCTGATCCGGGGGCGGACGGCGTCTGCATTCC 1520
CTGCCAGCCAGGTGAGCCGGGCCAGCTGGTGGGCCGCGATC 1560
ATCCAGAAAGACCCCTGCGCCGCTTCGATGGCTACCTCA 1600

1610      1620      1630      1640
.....
ACCAGGGCGCCAACAACAAGAAGATTGCCAAGGATGTCTT 1640
CAAGAAGGGGGACCAGGCCTACCTTACTGGTGATGTGCTG 1680
GTGATGGACGAGCTGGGCTACCTGTACTTCCGAGACCGCA 1720
CTGGGGACACGTTCCGCTGGAAAGGTGAGAACGTGTCCAC 1760
CACCAGAGGTGGAAGGCACACTCAGCCGCTGCTGGACATG 1800

1810      1820      1830      1840
.....
GCTGACGTGGCCGTGTATGGTGTGAGGTGCCAGGAACCG 1840
AGGGCCGGGCGGAATGGCTGCTGTGGCCAGCCCCACTGG 1880
CAACTGTGACCTGGAGCGCTTTGCTCAGGTCTTGGAGAAG 1920
GAACTGCCCCGTGTATGCGCGCCCCATCTTCTGCGCCTCC 1960
TGCCTGAGCTGCACAAAACAGGAACCTACAAGTTCCAGAA 2000

2010      2020      2030      2040
.....
GACAGAGCTACGGAAGGAGGGCTTTGACCCGGCTATTGTG 2040
AAAGACCCGCTGTTCTATCTAGATGCCCAGAAGGGCCGCT 2080
ACGTCCCGCTGGACCAAGAGGCCTACAGCCGCATCCAGGC 2120
AGGCGAGGAGAAGCTGTGATTCCCCCATCCCTCTGAGGG 2160
CCGGCGGATGCTGGATCCGGAGCCCCAGGTTCCGCCCCAG 2200

2210      2220      2230      2240
.....
AGCGGTCTTGGACAAGGCCAGACCAAAGCAAGCAGGGCCT 2240
GGCACCTCCATCCTGAGGTGCTGCCCCCTCCATCCAAACT 2280
GCCAAGTGACTCATTGCCTTCCCAACCTTCCAGAGGCTT 2320
TCTGTGAAAGTCTCATGTCCAAGTTCCGTCTTCTGGGCTG 2360
GGCAGGCCCTCTGGTTCCAGGCTGAGACTGACGGGTTTT 2400

2410      2420      2430      2440
.....
CTCAGGATGATGCTTTGGGTGAGGGTAGGGAGAGGACAAG 2440
GGGTACCCGAGCCCTTCCAGAGAGCAGGGAGCTTATAAA 2480
TGAACACAGAGCAGAAGTCCCCAGACTCAGGAAGTCAACA 2520
GAGTGGGCAGGGACAGTGGTAGCATCCATCTGGTGGCCAA 2560
AGAGAAATCGTAGCCCCAGAGCTGCCCCAAGTCACTGGGCT 2600
```

Fig. 50B

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hsFATP4 full length

2610	2620	2630	2640
CCACCCACCTCCAGGAGGGGAGGAGGACCTGACATC	2640		
TGTAGGTGGCCCTGATGCCCCATCTACAGCAGGAGGTCA	2680		
GGACCACGCCCCTGGCCTCTCCCCACTCCCCATCCTCCT	2720		
CCCTGGGTGGCTGCCTGATTATCCCTCAGGCAGGGCCTCT	2760		
CAGTCCTTGTGGGTCTGTGTCACCTCCATCTCAGTCTTGG	2800		
2810	2820	2830	2840
CCTGGCTATGAGGGGAGGAGGAATGGGAGAGGGGGCTCAG	2840		
GGGCCAATAAACTCTGCCTTGAGTCCTCTAAAAAAAAAA	2880		
AAAAAAAAAAAAAAAAAAAAAAAAAAAA	2907		

Fig. 50C

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hsFATP4 full length. protein

10 20 30 40  
MLLGASL<sup>10</sup>GVLLFSKLVKLPWTVQVGFSLFLYLGGGWR 40  
FIRVFIKTIRROIFGGLVLLKVKAKVROCLQERRTVPILF 80  
ASTVRRHPDKTALIFEGTDTHWTFROLDEYSSSVANFLOA 120  
RGLASGDVAAIFMENRNEFVGLWLGMAKLGVEAALINTNL 160  
RRDALLHCLTTSRARLVFGSEMASAICEVHASLDPSLSL 200  
210 220 230 240  
FCSGSWEPEGAVPPSTEHLDPLLKDAPKHLPSCPDKGFTDK 240  
LFYIYTSGTTGLPKAAIVVHSRYRMAALVYYGFRMRPND 280  
IVYDCLPLYHSAGNIVGIGQCLLHGMTVVIRKKFSASRFW 320  
DDCIKYNCTIVQYIGELCRYLLNOPPREAENQHQVRMALG 360  
NGLRQSIWTFNFSRFHIPQVAEFYGATECNCSLGNFDSOV 400  
410 420 430 440  
GACGFNSRI<sup>410</sup>LSFVYPIRLVRYNEDTMELIRGPDGVCIPCO 440  
PGEPGQLVGR<sup>420</sup>I IQKDPLRRFDGYLNOGANNKKIAKDYFKK 480  
GDQAYLTGDVLMDELGYLYFRDRTGDTFRWKGENVSTTE 520  
VEGTLSRLLDMADVAVYGVEVPGTEGRAGMAAVASPTGNC 560  
DLERFAQVLEKELPLYARPIFLRLLPELHKTGT<sup>430</sup>YKFQKTE 600  
610 620 630 640  
LRKEGFDP<sup>610</sup>AI VKDPLFYLDAQKGRYVPLDQEAYSRIQAGE 640  
EKL 643

Fig. 51

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&gt;hsFATP5(partial)

GTCGTTGGGATCCTCGGCTGCTTAGATCTCGGAGCCACCTGTGTTCTGGCCCCAAG  
TTCTCTACTTCCTGCTTCTGGGA  
TGACTGTCGGCAGCATGGCGTGACAGTGATCCTGTATGTGGGCGAGCTCCTGCGATA  
CTTGTGTAACATTCCCCAGCAAC  
CAGAGGACCGGACACATACAGTCCGCCTGGCAATGGGCAATGGACTACGGGCTGAT  
GTGTGGGGAGACCTTCCAGCAGCG  
TTTCGGTCCTATTTTCGGATCTNNGGAAGTCTTACGGGCTTCCACAGAAGGGCAACAT  
GGGGCTTTAGTTCAAATATTGTT  
GGGGGCGCTGCGGGGCCCTGGGGGCAAAGATGGAGCTTGCCTCCTCCGAATGCTGT  
CCCCCTTTGAGCTGGTGCAGTTCG  
ACATGGAGGCGGCGGAGCCTGTGAGGGACAATCAGGGCTTCTGCATCCCTGTAGGG  
CTAGGGGAGCCGGGGCTGCTGTTG  
ACCAAGGTGGTAAGCCAGCAACCCTTCGTGGGCTACCGCGGCCCCCGAGAGCTGTC  
GGAACGGAAGCTGGTGCACAACGT  
GCGGCAATCGGGCGACGTTTACTACAACACCGGGGACGTAAGTGGCCATGGACCGCG  
AAGGCTTCCTCTACTTCCGCGACC  
GACTCGGGGACACCTTCCGATGGAAGGGCGAGAACGTGTCCACGCACGAGGTGGAG  
GGCGTGTTGTGCGCAGGTGGACTTC  
TTGCAACAGGTTAACGTGTATGGCGTGTGCGTGCCAGGTTGTGAGGGTAAGGTGGGC  
ATGGCTGCTGTGGCATTAGCCCC  
CGGCCAGACTTTTCGACGGGGAGAAGTTGTACCAGCACGTTTCGCGCTTGGCTCCCTGC  
CTACGCTACCCCCCATTTTCATCC  
GCATCCAGGACGCCATGGAGGTCACCAGCACGTTCAAAGTGAAGACCCGGTTG  
GTGCGTGAGGGCTTCAATGTGGGG  
ATCGTGTTGACCCTCTGTTTGTACTGGACAACCGGGGCCAGTCCTTCCGGCCCCCTG  
ACGGCAGAAATGTACCAGGCTGT  
GTGTGAGGGAACCTGGAGGCTCTGATCACCTGGCCAACCCACTGGGGTAGGGATCA  
AAGCCAGCCACCCCCACCCAACA  
CACTCGGTGTCCCTTTCATCCTGGGCCTGTGTGAATCCAGCCTGGCCATACCCTCA  
ACCTCAGTGGGCTGGAAATGACA  
GTGGGCCCTGTAGCAGTGGCAGAATAAACTCAGMTGYGTTACAGAAA

Fig. 52

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hsFATP5partial.protein

10 20 30 40  
VVGILGCLDLGATCVLAPKFSTSCFWDDCRQHGVTVILYV 40  
GELLRYLCNIPQOPEDRTHTVRLAMGNGLRADVWGDLPAA 80  
FRSYFGSXEVLRASLEGQHGALVQILLGALRGPGGKDGAC 120  
LLRMLSPFELVQFDMEAAEPVRDNQGFVIPVGLGEPGLLL 160  
TKVVSQPPFVGYRGPRELSEKLVNRNVRSGDYNTGDV 200  
210 220 230 240  
LAMDREGFLYFRDRLGDTFRWKGENVSTHEVEGVLSQVDF 240  
LQQVNVYGVCPGCEGKVGMAAVALAPGOTFDGEKLYOHV 280  
RAWLPAYATPHFIRIQDAMEVTSTFKLMKTRLVREGFNVG 320  
IVVDPLFVLONRAQSFRPLTAEMYQAVCEGTWRL 354

Fig. 53

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hsFATP6 full lenght.DNA

10 20 30 40  
AACGGCAAGTAAGCGCAACGCAATTAATGTGAGTAGCTCA 40  
CTCATTAGGCACCCAGGCTTTACACTTTATGCTTCCGGG 80  
CTCGTATGTTGTGTGGAATTGTGAGCGGATACCAATTTCA 120  
CACAGGAACCAAGCTATGACATGATTACGAATTTAATACGA 160  
CTCACTATAGGGAATTTGGCCCTCGAGGCCAAGAATTCGG 200  
210 220 230 240  
CAGGAGGGGTGCTGAGCCCCTGCGCGGTTTCTGGTGCGTA 240  
GAGACTGTAAATCGCTGCGCTTCTCAGTCATCATCATCCC 280  
AGCTTTTCCGGCTCGAATTCAGCCTCCAACCTCAAGCTCG 320  
CGGGAAGACTACCTGAGAGGAGAAAAGCTTCTGTCCCTG 360  
GACCTTCTTCTGAGGGTGGAGTCGGAGGCTCCCTGCTTTC 400  
410 420 430 440  
CAGCCGCCCAGTGACCCAAGCTTAATCTTCAGCACCACCT 440  
GGGGCGACCTTTTCGGTGCAAACCTACGATTCTGTTTCTC 480  
AGGATTCTCCCATCCCGCTTCGCCCCGAAAAGCTGAC 520  
AAGAACTTCAGGTGTAAGCCCTGAGTAGTGAGGATCTGCG 560  
GTCTCCGTGGAGAGCTGTGCCTGGAAGAGAAGGACGCTGG 600  
610 620 630 640  
TGGGGGCTGAGATCAGAGCTGTCTTCTGGCCAGTTGCC 640  
CCATGCTTCTGTGATGGCTAACAGTTCTAGGGGCTGGAAT 680  
GGTCGCTGCACCTTCTTGCAAGAACTCCTGTTCCTTAC 720  
TTTTGGGATGACTTCTGGTTCGTGTTGAAGGTGGTGCTCA 760  
TTATAATTCGGCTGAAGAAGTATGAAAAGAGAGGGGAGCT 800  
810 820 830 840  
GGTGACTGTGCTGGATAAATCTTGAGTCATGCCAAAAGA 840  
CAACCTCGGAAACCTTTTCATCATCTATGAGGGAGACATCT 880  
ACACCTATCAGGATGTAGACAAAAGGAGCAGCAGAGTGGC 920  
CCATGTCTTCTGAACCATTCCTCTCTGAAAAAGGGGGAC 960  
ACGGTGGCTCTGCTGATGAGCAATGAGCCGGACTTCGTT 1000  
1010 1020 1030 1040  
ACGTGTGGTTCGGCCTCGCCAAGCTGGGCTGCGTGGTGGC 1040  
CTTTCTCAACCAACATTGCTCCAACCTCCCTCCTGAAT 1080  
TGCATCCGCGCTGTGGGCCCAGAGCCCTAGTGGTGGGCG 1120  
CAGATTTGCTTGGAACGGTAGAAGAAATCCTTCCAAGCCT 1160  
CTCAGAAAATATCAGTGTTTGGGGGATGAAAGATTCTGTT 1200

Fig. 54A

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hsFATP6 full lenght.DNA

1210	1220	1230	1240
CCACAAGGTGTAATTTCACTCAAAGAAAACTGAGCACCT 1240			
CACCTGATGAGCCCGTGCCACGCAGCCACCATGTTGTCTC 1280			
ACTCCTCAAGTCTACTTGTCTTTACATTTTACCTCTGGA 1320			
ACAACAGGTCTACCAAAGCAGCTGTGATTAGTCAGCTGC 1360			
AGGTTTTAAGGGGTTCTGCTGTCTGTGGGCTTTTGGTTG 1400			
1410	1420	1430	1440
TACTGCTCATGACATTGTTTATATAACCCCTTCCTCTGTAT 1440			
CATAGTTCAGCAGCTATCCTGGGAATTTCTGGATGTGTTG 1480			
AGTTGGGTGCCACTTGTGTGTTAAAGAAGAAATTTTCAGC 1520			
AAGCCAGTTTTGGAGTGACTGCAAGAAGTATGATGTGACT 1560			
GTGTTTCAGTATATTGGAGAACTTTGTCGTACCTTTGCA 1600			
1610	1620	1630	1640
AACAACTCTAAGAGAGAAGGAGAAAAGGATCATAAGGTGCG 1640			
TTTGCAATTGGAAATGGCATACGGAGTGATGTATGGAGA 1680			
GAATTTTTAGACAGATTTGGAAATATAAAGGTGTGTGAAC 1720			
TTTATGCAGCTACCGAATCAAGCATATCTTTCATGAAC TA 1760			
CACTGGGAGAATTGGAGCAATTGGGAGAACAAATTTGTTT 1800			
1810	1820	1830	1840
TACAAACTTCTTTCCACTTTTGTACTTAATAAAGTATGACT 1840			
TTCAGAAAGATGAACCCATGAGAAATGAGCAGGGTTGGTG 1880			
TATTCATGTGAAAAAAGGAGAACCTGGACTTCTCATTTCT 1920			
CGAGTGAATGCAAAAAATCCCTTCTTTGGCTATGCTGGGC 1960			
CTTATAAGCACACAAAAGACAAATTGCTTTGTGATGTTTT 2000			
2010	2020	2030	2040
TAAGAAGGGGAGATGTTTACCTTAATACTGGAGACTTAATA 2040			
GTCCAGGATCAGGACAATTTCTTTATTTTTGGGACCGTA 2080			
CTGGAGACACTTTCAGATGGAAAGGAGAAAATGTCGCAAC 2120			
CACTGAGGTTGCTGATGTTATTGGAATGTTGGATTTCATA 2160			
CAGGAAGCAAACGTCTATGGTGTGGCTATATCAGGTTATG 2200			
2210	2220	2230	2240
AAGGAAGAGCAGGAATGGCTTCTATTATTTTAAACCAAA 2240			
TACATCTTTAGATTTGGAAAAAGTTTATGAACAAGTTGTA 2280			
ACATTTCTACCAGCTTATGCTTGTCCACGATTTTAAAGAA 2320			
TTCAGGAAAAAATGGAAGCAACAGGAACATTCAAAC TATT 2360			
GAAGCATCAGTTGGTGGAGATGGATTTAATCCACTGAAA 2400			
2410	2420	2430	2440
ATTTCTGAACCACTTTACTTTCATGGATAACTTGAAAAAGT 2440			
CTTATGTTCTACTGACCAGGGAACCTTTATGATCAAATAAT 2480			
GTTAGGGGAAATAAACTTTAAGATTTTTATATCTAGAAC 2520			
TTTCATATGCTTTCTTAGGAAGAGTGAGAGGGGGGTATAT 2560			
GATTCCTTATGAAATGGGGAAAGGGAGCTAACATTAATTA 2600			

Fig. 54B



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hsFATP6 full lenght.DNA

2610	2620	2630	2640
TGCATGTACTATATTTCTTAATATGAGAGATAATTTTT 2640			
AATTGCATAAGAATTTTAATTTCTTTTAATTGATATAAAC 2680			
ATTAGTTGATTATTCCTTTTATCTATTTGGAGATTCAGTG 2720			
CATAACTAAGTATTTCTTAATACTAAAGATTTTAAATA 2760			
ATAAATAGTGGCTAGCGGTTTGGACAATCACTAAAAATGT 2800			
2810	2820	2830	2840
ACTTTCTAATAAGTAAAAATTTCTAATTTTGAATAAAAGAT 2840			
TAAATTTTACTGAAAAAAAAAAAAAAAAAAAAAATTGGCG 2880			
GCCGC 2885			

Fig. 54C

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hsFATP6 full lenght.protein

```
      10      20      30      40
MLLSWLTVLGAGMVVLHFLQKLLFPYFWDDFWFLKVVLI 40
IIRLKKEKRGELVTVLQKFLSHAKRQPRKPFIIYEGDIY 80
TYQDVQKRSSRVAVHVLNHSLLKKGDTVALLMSNEPDFVH 120
VWFGAKLGCYVAFLENTNIRSNLLNCIRACGPRALVGA 160
DLLGTVEEILPSLSENI SVWGMKDSVPGVISLKEKLST 200
      210      220      230      240
PDEPVPRSHHVVSLLKSTCLYIFTSGTTGLPKAAVISQLQ 240
VLRGSAVLWAFGCTAHDIVYITLPLYHSSAAILGISGCV 280
LGATCVLKKKFSASQFWSQCKKYDVTVFQYIGELCRYLCK 320
QSKREGEKDHKVRLAIGNGIRSDVWREFLDRFGNIKVC 360
YAATESSISFMNYTGRIGAIGRTNLFYKLLSTFDLIK 400
      410      420      430      440
QKDEPMRNEQGWCIHYKKGEPGLLISRVNAKNPFFGYAGP 440
YKHTKDKLLCDVFKKGDVYLNLTGDLIVQDQDNFLYFW 480
GDTFRWKGENVATTEVADVIGMLDFIQEANVYGVAISGY 520
GRAGMASIILKPNTSLDEKVEQVVTFLPAYACPRFLRI 560
QEKMEATGTFKLLKHQLVEDGFNPLKISEPLYFMONLKK 600
      610      620      630      640
YVLLTRELYDQIMLGEIKL 620
```

Fig. 55

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mFATP1 full length.DNA

```

      10      20      30      40
      |      |      |      |
AAGTTCCTCCACTCCAGACTTCTGCGAGAACCCGTGAGGAAG 40
CAGCGAGAACCGGGGGTTTGAAGCCAGAGAAGGATGCGG 80
ACTCCGGGAGCAGGAACAGCCTCTGTGGCCTCATTGGGGC 120
TGCTTTGGCTTCTGGGACTTCCGTGGACCTGGAGCGCGGC 160
GGCGGCGTTTCGGTGTGTACGTGGGTAGCGGTGGCTGGCGA 200
      210      220      230      240
      |      |      |      |
TTTCTGCGTATCGTCTGCAAGACGGCGAGGCGAGACCTCT 240
TTGGCCTCTCTGTTCTGATCCGCGTGGCGCTAGAGCTACG 280
ACGACACCGGCGAGCAGGAGACAGATCCCACGCATCTTC 320
CAGGCCGTGGCCAGCGACAGCCGGAGCGCCTGGCGCTGG 360
TAGATGCGAGTAGCGGTATCTGCTGGACCTTCGCACAGCT 400
      410      420      430      440
      |      |      |      |
AGACACCTACTCCAATGCTGTGGCCAATCTGTTCTCCAG 440
CTGGGCTTTGCGCCAGGCGATGTGGTGGCTGTGTTCTGG 480
AAGGCCGGCCCGAGTTTCGTGGGACTGTGGCTGGGCCTGGC 520
CAAGGCCGGTGTAGTGGCTGCGCTTCTCAATGTCAACCTG 560
AGGCCGGGAGCCCCCTTGCTTCTGCTTGGGCACATCAGCTG 600
      610      620      630      640
      |      |      |      |
CCAAGGCCCTCATTTATGGCGGGGAGATGGCAGCGGCGGT 640
GGCGGAGGTGAGTGAGCAGCTGGGGAAGAGCCTGCTCAAG 680
TTCTGCTCTGGAGATCTGGGGCCTGAGAGCGTCTGCCTG 720
ACACGCAGCTTCTGGACCCCATGCTTGCTGAGGCGCCAC 760
CACACCCCTGGCACAGGCCCCAGGCAAGGGCATGGATGAT 800
      810      820      830      840
      |      |      |      |
CGGCTATTTTACATCTATACTTCTGGGACCACCGGACTTC 840
CTAAGGCGGCCATTGTGGTGCACAGCAGGTACTACCGCAT 880
CGCAGCCTTCGGCCACCATTCCTACAGCATGCGGGCCAAC 920
GATGTGCTCTATGACTGCCTACCTCTCTACCACTCAGCAG 960
GGAACATCATGGGCGTGGGACAGTGTATCATCTACGGGTT 1000
      1010      1020      1030      1040
      |      |      |      |
AACGGTGGTACTGCGCAAGAAGTTCTCCGCCAGCCGCTTC 1040
TGGGACGACTGTGTCAAATATAATTGCACGGTAGTGCACT 1080
ACATCGGTGAAATATGCCGCTACCTGCTAAGGCAGCCGGT 1120
TCGCGATGTAGAGCGGCGGCACCGCGTGCGCCTGGCCGTG 1160
GGTAACGGACTGCGGCCAGCCATCTGGGAGGAGTTACGC 1200

```

Fig. 56A

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mFATP1 full length.DNA

```
1210 1220 1230 1240
AGGGTTTCGGTGTGCGACAGATTGGCGAGTTCTACGGCGC 1240
CACCGAATGCAACTGCAGCATTGCCAACATGGACGGCAAG 1280
GTCGGCTCCTGCGGCTTCAACAGCCGTATCCTCACGCATG 1320
TGTACCCCATCCGTCTGGTCAAGGTCAACGAGGACACGAT 1360
GGAGCCACTGAGGGACTCCCAAGGCCTCTGCATCCCCTGC 1400

1410 1420 1430 1440
CAGCCCGGGGAACCTGGGCTTCTCGTGGGCCAGATCAACC 1440
AGCAAGACCCTCTGCGGCGCTTCGATGGCTATGTTAGTGA 1480
CAGCGCCACCAACAAGAAGATTGCCCACAGCGTGTTCGA 1520
AAGGGGACAGCGCCTACCTTTCAGGTGACGTGCTAGTGA 1560
TGGACGACTGGGGTACATGTACTTCCGTGACCGCAGCGG 1600

1610 1620 1630 1640
GGATACCTTCCGATGGCGCGGGCGAGAACGTATCCACCACG 1640
GAGGTGGAAGCCGTGCTGAGCCGCCCTGTTGGGCCAGACGG 1680
ACGTGGCTGTGTATGGAGTGGCTGTGCCAGGAGTGGAGGG 1720
GAAAAGCGGCATGGCGGCCATTGCAGACCCCCACAACCAG 1760
CTGGACCCTAACTCAATGTACCAGGAATTGCAGAAGGTTT 1800

1810 1820 1830 1840
TTGCATCCTATGCCAGCCCATCTTCCTGCGTCTTCTGCC 1840
CCAAGTGGATACAACAGGCACCTTCAAGATCCAGAAGACC 1880
CGACTACAGCGTGAAGGCTTTGACCCCCGCCAGACCTCAG 1920
ACCGGCTCTTCTTTCTAGACCTGAAACAGGGACGCTACCT 1960
ACCCCTGGATGAGAGAGTCCATGCCCGCATCTGCGCAGGC 2000

2010 2020 2030 2040
GACTTCTCACTCTGAGCCTGGTGAGTGGGATGGCCCTGGA 2040
CTTGTGAGACCAGGGAGCCGGACACCCCTGTTCAAGTGT 2080
TCTCCTGCCCTGGCCACGTGGCCAGCAGCACCTGTGGGTGC 2120
AGGAAACTGGAACCTGAGTGGCCGGGTGTCCCTTTCCTAC 2160
AACCACCATGCACACATCTAGCCTCTGCCTTGGTCTTTT 2200

2210 2220 2230 2240
TCTCCATCTCTTTCCTCCGTGCCAGCAGGAGCCCCACAG 2240
ACACATTGGCTGCTGTGTCCTGCAGTGGGACCGGTGTCTA 2280
GGGGTCCATGCTGCAGGCTGTGACCCGCACTGGTGCCAC 2320
CTCCCTTCCCCATTGTGCCTTAGGTTCTCCACTGTGCGC 2360
CGGTGAAGCAAGTGGGGACCCACATAGCTGTTGTCCCTGC 2400

2410 2420 2430 2440
TGAGGGTTGGTAGCAAAATGCACCCTCATGTCAGCTGGGAG 2440
ACACATGCAGTCTCCCACTGACCCCCAATCAACTGAAGAT 2480
ACTGTTTGTATTATTGTTTTGAGATAGGGTCTCACTGTG 2520
GAGGCCAAGCTGGCCTCAGGCTCACCCTCTACTGCCTCC 2560
GGGCACCAGCCTGCAGTTTGATGACATGTATGCACTATTG 2600
```

Fig. 56B

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mFATP1 full length.DNA

```
      2610      2620      2630      2640
TTCTAAGGGTCTTCTGAGTCCCTGCTTTCCCCTCATGTCC 2640
TAAACCTTCCAGAACTGACTCTGATCACTTGGATGTAGC 2680
TAGTGTGGCCCTGCCCACGTGTGTCAATTCAGGGGTCCC 2720
CAGGCATCATCTCTGGAGGCCCTAACCTTGGCAAAGCTTG 2760
GATGTCCTCACATCACAGCAGGAGACCCAGGAAGGTTGCT 2800

      2810      2820      2830      2840
GTGGTGTCTCTTGGGCACCCCTGGCGGCAGCCGTGGACAT 2840
GCTTCCCTGCTGTGATAGCCCCAACTGTTGCCTATGACAT 2880
TTGAGGTCTACCCTTCTGGCTGCCATGGTCCCCATTGAGA 2920
TCTTTGGTGACTCACCTCAGCCACCAAGCCAGGCCTCTGC 2960
CTTCCTTCAGCTCTAAGGGCATGAAGGGTGTGGACAGAGC 3000

      3010      3020      3030      3040
AGCCACAGGCTGCCCACAGTCACCCACATGCAAGTGTTAT 3040
TTCCTTGTGTTTAAAAAATAAACATGCTGAGCCTTG 3080
AAAAAAAAAAAAAAAAAAAA 3098
```

Fig. 56C

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mFATP1 full lenght.protein

10 20 30 40  
MRTPGAGTASVASLGLLWLLGLPWTWSAAAAFGVYVGS GG 40  
WRFLRIVCKTARRDLFGLSVLIRVRLELRRHRRAGDTIPR 80  
IFQAVAQRQPERLALVDASSGICWTF AOLDTYSNAVANLF 120  
LQLGFAPGDVVAVFLEGRPEFVGLWLGLAKAGVVAALLNV 160  
NLRREPLAFCLGTSAAKALIYGGEMAAVAEVSEQLGKSL 200

210 220 230 240  
LKFCSGDLGPESVLPDTOLLDPMLAEAPTTPLAQAPGKGM 240  
DDRLFYIYTS GTTGLPKAAIVVHSRYRIA AAFGHHSYS MR 280  
ANDVLYDCLPLYHSAGNIMGVGCIIYGLTVVLRKKFSAS 320  
RFWDDCVKYNCTVVQYIGEICRYLLROPYRDVERRHRVRL 360  
AVGNGLRPAIWEEFTOGFGVRQIGEFYGATECNCSIANMD 400

410 420 430 440  
GKYVSGCGFNSRILTHVYPIRLVKVNEOTMEPLRDSQGLCI 440  
PCQPGEPGLLVGQINQODPLRRFDGYVSDSATNKKIAHSV 480  
FRKGDSAYLSGDVLYMDELGYMYFRDRSGDTFRWRGENYS 520  
TTEVEAVLSRLLGQTDVAVYGVAVPGVEGKSGMAAIAOPH 560  
NQLDPNSMYQELQKVLASYAOPIFLRLLPQVDTTGTFKIQ 600

610 620 630 640  
KTRLQREGFDPROTS DRLFFLDLKOGRYLPLDERVHARIC 640  
AGDFSL. 647

Fig. 57

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mVLACS(FATP2)full length.DNA

```

      10      20      30      40
GACACAGTACTGCCGATGTTGGACAGAGGATCGCTTAACA 40
GAACGAAATCTCAAAACAAATTAACAGGACCCGGTTGCTT 80
GATTTCCCAAATCAGAAAAGGCTCGAAATGTCTAGAGGGG 120
CTGACTGATGCAGCGGTGACCCGGACTGGAGACAGTTGGA 160
CGCGATCATCTCTGGTGCTTTTGTTCACCTTGAAACCTT 200

      210      220      230      240
CGCCACAGGAGACTTGCTTGAGCAGAGAAGCAAACGTGGA 240
GAAACAAAGAGAGATCTAGCGAAAAGCCTCTGGGACCAAG 280
GAGGGGAGGTGGGACTCTGGGTTGGCGGTGGCACCTGCTG 320
CCGGCTATTAATAATAGGGTCGCGATGCGTTTATAAGGTG 360
TTTGATTAAACAAAGACTCTATGAGAGAAGAATAACTAGC 400

      410      420      430      440
AACAGCCCCACGTCTGAGTCGTCGCCTCCGACCTTTTTCA 440
ACGTGGGTTCTTTGGGCCGAGCGTCGTTTGCCGAGAACTA 480
GATCTCACCTGACCCCAGACGCTGAAAACAAGCGCTGTGG 520
CATCCTGGGCCACCCAAGCTGACAAGGGCGCGCCCCCTGA 560
GCACACGAGGTGCCCCACGAGGGGGAGGGACCCACAGCCG 600

      610      620      630      640
TCCCGCCCCGACCCGCGGTGTCCGCTGCGGGCACCTGCAGC 640
CGAGCCGCCACCCGAGTCGCAGCGCGTCCGGCGGGCGAA 680
CCCGGTCTGTACGTCGTCAGCACCTGCTCTGCTTCTCTCC 720
CGCCCGCCGCGCGCTGCACGCCCTCGAGCGCTCCCTCGGC 760
CCCGGCGGGGACCGGGGACCCCGCAGCCACCGCCATGCTG 800

      810      820      830      840
CCTGTGCTCTACACCGGCCTGGCGGGGCTGCTGCTGCTGC 840
CTCTGCTGCTCACCTGCTGCTGCCCTACCTCTCCAGGA 880
CGTGCGGTTCTTCCTGCAACTGGCCAACATGGCCCGGCAG 920
GTGCGCAGCTACCGGCAGCGGCGACCCGTGCGCACCATCC 960
TGCATGTCTTCTTGGAGCAAGCGCGCAAGACCCCGCACA 1000

      1010      1020      1030      1040
GCCCTTCTGCTGTTTTCGCGACGAGACGCTTACCTACGCC 1040
CAGGTAGACCGGCGCAGCAACCAAGTAGCGCGAGCGCTGC 1080
ATGATCACCTGGGCCTGCGGCAGGGGGATTGCGTGGCCCT 1120
CTTCATGGGCAATGAGCCGGCTACGTGTGGCTCTGGCTG 1160
GGACTGCTCAAAC TGGGCTGTCCCATGGCGTGCTCAACT 1200

```

Fig. 58A

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mVLACS(FATP2)full length.DNA

1210	1220	1230	1240
ACAACATCCGTGCCAAGTCTCTGCTACACTGCTTTTCAGTG 1240			
CTGCGGGGCGAAGGTGCTGCTGGCCTCCCCAGAGCTACAC 1280			
GAAGCTGTCGAGGAGGTTCTTCCAACCTGAAAAAGGAGG 1320			
GCGTGTCGGTCTTCTACGTAAGCAGAATTCTAACACTAA 1360			
TGGCGTGGACACAGTACTGGACAAAGTAGACGGGGTGTCG 1400			
1410	1420	1430	1440
GCGGACCCCATCCCGGAGTCTGTGGAGGTCTGAAGTCACGT 1440			
TCACCACACCCGCAGTCTACATATATACTTCGGGCACCAC 1480			
AGGTCTTCCAAAGGCTGCAACCATTAATCACCATCGCCTC 1520			
TGGTATGGGACCAGCCTTGCCCTGAGGTCCGGAATTAAGG 1560			
CTCATGACGTCATCTACACCACCATGCCCTGTACCACAG 1600			
1610	1620	1630	1640
CGCGGCGCTCATGATTGGCCTCCACGGATGCATTGTGGTT 1640			
GGGGCTACATTTGCTTTGCGGAGCAAATTTTCAGCCAGCC 1680			
AGTTTTGGGACGACTGCAGGAAATACAACGCCACTGTCTAT 1720			
TCAGTACATCGGTGAACTGCTTCGGTACCTCTGCAACACG 1760			
CCCCAGAAACCAAATGACCGGGACCACAAAGTGAAAAATAG 1800			
1810	1820	1830	1840
CACTAGGAAATGGCTTACGAGGAGATGTGTGGAGAGAGTT 1840			
CATCAAGAGATTTGGGGACATTCACATTTATGAGTTCTAC 1880			
GCTTCCACTGAAGGCAACATTGGATTTATGAACTATCCAA 1920			
GAAAAATCGGAGCTGTTGGAAGAGAAAATTACCTACAAAA 1960			
AAAAGTTGTAAGGCACGAGCTGATCAAGTATGACGTGGAG 2000			
2010	2020	2030	2040
AAGGATGAGCCTGTCCGTGATGCAAATGGATATTGCATCA 2040			
AAGTCCCCAAAGGAGAGGTTGGACTCTTGATTTGCAAAAT 2080			
CACAGAGCTCACACCATTTTTTGGCTATGCTGGAGGAAAG 2120			
ACCCAGACAGAGAAGAAAAAGCTCAGAGATGTTTTTAAGA 2160			
AAGGAGACGTCTACTTCAACAGTGGCGATCTCTGATGAT 2200			
2210	2220	2230	2240
CGACCGTGAAAATTTTCATCTATTTTCACGACAGAGTTGGA 2240			
GACACCTTCCGGTGAAAGGAGAGAATGTAGCTACCACGG 2280			
AAGTCGCTGACATTGTGGGACTGGTAGATTTTGTGAAGA 2320			
AGTGAATGTTTACGGTGTGCCCGTGCCAGGTCATGAAGGT 2360			
CGCATCGGGATGGCCTCGATCAAGATGAAAGAAAACTACG 2400			
2410	2420	2430	2440
AGTTCAATGGAAAGAACTCTTTCAGCACATCTCGGAGTA 2440			
CCTGCCCACTTACTCGAGGCCTCGGTTTCTGAGAATACAA 2480			
GATACCATTTGAGATCACCGGGACTTTTAAACACCGCAAAG 2520			
TGACCTTGATGGAAGAGGGCTTTAACCCCTCAGTCATCAA 2560			
AGATACCTTGATTTTTCATGGATGACACAGAAAAACATAC 2600			

Fig. 58B



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mVLACS(FATP2)full length.DNA

2610                      2620                      2630                      2640  
 GTGCCATGACTGAGGACATTTATAATGCCATAATTGATA 2640  
 AGACTCTGAAGCTCTGAATGTTGCCTGGCTCCTAACACTT 2680  
 CAGAAAGAACACCAATAGGCCCTAGCATAGCCCTTCACA 2720  
 TGTGTAATCCAACCTTTAACTTGATTAAGGTTTATAGGTGT 2760  
 GATTTTTCTAGGAAATTATTCATTTAAAGGACAATTGTT 2800  
  
 2810                      2820                      2830                      2840  
 TGTTTGTTTGTTTGTTTTTATTAATTACACCAGAACGTT 2840  
 TGCAAGTAAAAAGATTTAAAGTCACCTATTTTTCAATGTG 2880  
 CACCTGCCATTTGTCCTTGCAAACCTTAGCTTCTTGGAGAG 2920  
 AGCGCCTATTTTTTTTAAAGACATAATAAACTATGTAAAC 2960  
 ACT 2963

Fig. 58C

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mVLACS(FATP2)full length.prot

```
      10      20      30      40
MLPVLYTGLAGLLLLPLLLTCCCPYLLQDVRFLLQLANMA 40
RQVRSYRORRPVRTILHVFLEQARKTPHKPFLLFRDETLT 80
YAQVDRRSNQVARALHDHLGLRGDCVALFMGNEPAYVWL 120
WLGLLKLGCPMACLNYNIRAKSLLHCFCCGAKVLLASPE 160
LHEAVEEVLP TLKKEGVSVFYVSRTSNTNGVDTVLDKVDG 200
      210      220      230      240
VSADPIPESWRSEVTFITPAVYIYTS GTTGLPKAATINHH 240
RLWYGTSLALRSGIKAHDVIYTTMP LYHSAALMIGLHGCI 280
VVGATFALRSKF SASQFWDCRKYNATVIOYIGELLRYLC 320
NTPQKPNORDHKVKIALGNGLRGDVWREFIKRFGDIHIYE 360
FYASTE GNIGFMNYPRKIGAVGRENYLOKKVVRHEL IKYD 400
      410      420      430      440
VEKDEPV RDANGYCIKVPKGEVGLLICKITELTPFFGYAG 440
GKTQTEKKLRDVFKKGDVYFNSGDLLMIDRENFIYFHDR 480
VGDTFRWKGENVATTEVADIVGLVD FVEEVN VYGVPVPGH 520
EGRIGMASIKMKENYEFNGKKLFQHI SEYLPYSRPRFLR 560
IQDTIEITGTFKHKVTLMEEGFNPSVIKDTLYFMDDTEK 600
      610      620      630      640
TYVPMTEDIYNAIIDKTLKL 621
```

Fig. 59

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mFATP4 partial.DNA

```
      10      20      30      40
      |      |      |      |
GATCAGCTCTTCTATATCTACACGTCGGGCACACAGGGGC 40
TACCCAAAGCTGCCATTGTGGTGCACAGCAGGTATTACCG 80
AATGGCTGCCCTGGTGTACTATGGATTCCGCATGCGGCCT 120
GATGACATTGTCTATGACTGCCTCCCCCTCTACCACTCAG 160
CAGGAAACATTGTGGGGATTGGCCAGTGGTACTCCACGG 200
      210      220      230      240
      |      |      |      |
CATGACTGTGGTGATCCGGAAGAAGTTTTTCAGCCTCCCGG 240
TTCTGGGATGACTGTATCAAGTACAACGACAAATTGTAC 280
AGTACATTGGTGAGCTTTGCCGCTACCTCCTGAACCAGCC 320
ACCCCGTGAGGCTGAGTCTCGGCACAAGGTGCGCATGGCA 360
CTGGGCAACGGTCTCCGGCAGTCCATCTGGACCGACTTCT 400
      410      420      430      440
      |      |      |      |
CCAGCCGTTTCCACATTCCCAAGGTGGCCGAGTTCTACGG 440
GGCCACCGAGTGCAACTGTAGCTTGGGCAACTTTGACAGC 480
CAGGTGGGGGCTGTGGCTTCAATAGCCGCATCCTGTCCT 520
TTGTGTACCCCATCCGCTTGGTACGAGTCAATGAGGATAC 560
CATGGAAGTGTATCCGGGGACCCGATGGCGTCTGCATTCCC 600
      610      620      630      640
      |      |      |      |
TGTC AACAGGCCAGCCAGGCCAGCTGGTGGGTGCGATCA 640
TCCAGCAGGACCCCTACGCCGTTTTGATGGCTACCTCAA 680
CCAGGGTGCCAACAACAAGAAGATTGCTAGTGATGTCTTC 720
AAGAAAGGGGACCAAGCCTACCTCACTGGTGACGTGCTGG 760
TGATGGATGAGCTGGGCTACCTGTACTTCCGAGACCGCAC 800
      810      820      830      840
      |      |      |      |
AGGGGACACGTTCCGCTGGAAAGGGGAGAATGTGTCTACC 840
ACTGAAGTGGAGGGCACACTCAGCCGCCTGCTTCAGATGG 880
CAGATGTGGCTGTTTATGGTGTGAGGTGCCAGGAGCTGA 920
GGGCCGAGCAGGAATGGCTGCTGTGGCAAGCCCCACTAGC 960
AACTGTGACCTGGAGAGCTTTGCACAGACCTTGAAAAAGG 1000
      1010      1020      1030      1040
      |      |      |      |
AGCTGCCCCGTGACGCCCGCCCCATCTTCCTCCGCTTCTT 1040
GCCTGAGCTGCACAAAACAGGAACCTTCAAGTTCCAGAAG 1080
ACAGAGTTGCGGAAGGAGGGCTTTGACCCGTCTGTTGTGA 1120
AAGACCCACTCTTCTATTTGGATGCCCCGACAGGCTGCTA 1160
TGTTGCACCTGGACCAAGAGGCCTATACCCGCATCCAGGCA 1200
```

Fig. 60A

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mFATP4 partial.DNA

---

1210      1220      1230      1240

---

GGCGAGGAGAAGCTGTGATTTCCCCCACATCCCTCTGAGG 1240  
GCCAGAGGATGCTGGATTCAGAGCCCCAGCTTCCACTCCA 1280  
GAAGGGGTCTGGGCAAGGCCAGACCAAAGCTAGCAGGGCC 1320  
CGCACCTTCACCCTAGGTGCTGATCCCCCT 1350

Fig. 60B

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mFATP4partial.DNA

```
      10      20      30      40
DQLFYIYTS GTTGLPKAAIVVHSRYRMAALVYYGFRMRP 40
DDIVYDCLPLYHSAGNIVGIGOCVLHGMTVVIRKKFSASR 80
FWDDCIKYNCTIVQYIGELCRYLLNOPPREAESRHKYRMA 120
LGNGLRQSIWTD FSSRFHIPKVAEFYGATECNC SLGNFDS 160
QYGACGFNSRI LSFVYPIRLVRVNEDTMELIRGPDGVCIP 200
      210      220      230      240
COPGPGQLVGR I IQDPLRRFDGYLNOGANNKKIASDVF 240
KKGQQAYLTGD VLYMDELGYLYFRDRTGDTFRWKGENVST 280
TEVEGTLSRLL OMAADVAVYGVEVPGAEGRAGMAAVASPTS 320
NCOLESFAOTL KKKELPLYARPIFLRFLPELHKTGTFFKFK 360
TELKKEGFOPSV VKDPLFYLDARTGCYVALDQEA YTRIOA 400
      410      420      430      440
GEEKL. 406
```

Fig. 61

mmFATP1 full length.DNA 71/117

```
10      20      30      40
ATGCGGGCTCCTGGAGCAGGAACAGCCTCTGTGGCCTCAC 40
TGGCGCTGCTTTGGTTTCTGGGACTTCCGTGGACCTGGAG 80
CGCGCGCGCGCGCTTCTGTGTGTACGTGGGTGGCGGCGGC 120
TGGCGCTTTCTGCGTATCGTCTGCAAGACGGCGAGGCGAG 160
ACCTCTTTGGCCTCTCTGTTCTGATTCTGTTCGGCTAGA 200

210     220     230     240
GCTGCGACGACACCGGCGAGCAGGAGACGATCCCGTGC 240
ATCTTCCAGGCTGTGGCCCGGCGACAACCAGAGCGCCTGG 280
CACTGGTGGACGCCAGTAGTGGTATATGCTGGACCTTCGC 320
ACAGCTGGACACCTACTCCAATGCTGTAGCCAACCTGTTT 360
CGCCAGCTGGGCTTTGCACCAGGCGATGTGGTGGCTGTGT 400

410     420     430     440
TCCTGGAGGGCCGGCCGGAGTTCGTGGGACTGTGGCTGGG 440
CCTGGCCAAGGCCGGTGTGGTGGCTGCTCTTCTCAATGTC 480
AACCTGAGGCGGGAGCCCCTGGCCTTCTGCCTGGGCACAT 520
CAGCTGCCAAGGCCCTCATTTATGGCGGGGAGATGGCAGC 560
GGCGGTGGCGGAGGTGAGCGAGCAGCTGGGGAAGAGCCTC 600

610     620     630     640
CTCAAGTTCTGCTCTGGAGATCTGGGGCCTGAGAGCATCC 640
TGCTTGACACGCAGCTCCTGGACCCCATGCTTGCTGAGGC 680
GCCCCACCACCCCCTGGCACAAGCCCCAGGCAAGGGCATG 720
GATGATCGGCTGTTTTACATCTATACTTCTGGGACCACCG 760
GGCTTCTTAAGGCTGCCATTGTGGTGCACAGCAGGTACTA 800

810     820     830     840
CCGCATTGCTGCCTTTGGCCACCATTCCTACAGCATGCGT 840
GCCGCCGATGTGCTCTATGACTGCCTGCCACTCTACCACT 880
CTGCAGGGAACATCATGGGTGTGGGGCAGTGGCTCATCTA 920
CGGGTTGACGGTGGTACTGCGCAAGAAGTTCTCCGCCAGC 960
CGCTTCTGGGATGACTGTGTCAAGTACAATTGCACGGTAG 1000

1010    1020    1030    1040
TGGATGACATAGGTGAAATCTGCCGCTACCTGCTGAGGCA 1040
GCCGGTTCGCGACGTGGAGCAGCGACACCGCGTGCGCCTG 1080
GCCGTGGGTAATGGGCTGCGGCCAGCCATCTGGGAGGAGT 1120
TCACGCAGCGCTTCGGTGTGCCACAGATCGGCGAGTTCTA 1160
CGGCGCTACCGAGTGCAACTGCAGCATTGCCAACATGGAC 1200
```

Fig. 62A

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mmFATP1 full length.DNA

1210	1220	1230	1240
GGCAAGGTCGGCTCCTGCGGCTTCAACAGCCGTATCCTCA 1240			
CGCATGTGTACCCCATCCGTCTGGTCAAGGTCAATGAGGA 1280			
CACGATGGAGCCACTGCGGGACTCCGAGGGCCTCTGCATC 1320			
CCGTGCCAGCCCGGGGAACCCGGCCTTCTCGTGGGCCAGA 1360			
TCAACCAGCAGGACCCTCTGCGGCGTTTCGATGGTTATGT 1400			
1410	1420	1430	1440
TAGTGACAGTGCCACCAACAAGAAGATTGCCACAGCGTT 1440			
TTCCGAAAGGGCGATAGCGCCTACCTCTCAGGTGACGTGC 1480			
TAGTGATGGACGAGCTGGGCTACATGTATTTCCGTGACCG 1520			
CAGCGGGGACACCTTCCGCTGGCGCGGGGAGAACGTGTCC 1560			
ACCACGGAGGTGGAAGCCGTGCTGAGCCGCCCTACTGGGCC 1600			
1610	1620	1630	1640
AGACGGACGTGGCTGTGTATGGGGTGGCTGTGCCAGGAGT 1640			
GGAGGGGAAAGCTGGCATGGCAGCCATCGCAGATCCCCAC 1680			
AGCCAGTTGGACCCCTAACTCAATGTACCAGGAATTACAGA 1720			
AGGTTCTTGATCCTATGCTCGGCCCATCTTCCTGCGTCT 1760			
TCTGCCCCAGGTGGATACCACAGGCACCTTCAAGATCCAG 1800			
1810	1820	1830	1840
AAGACCCGGCTGCAGCGTGAAGGCTTTGACCCCCGTCAGA 1840			
CCTCAGACAGGCTCTTCTTTCTAGACCTGAAGTCCGGCAC 1880			
GAGGTATCTACCCCTGGATGAGAGAGTCCATGCCCGCATT 1920			
TGCGCAGGCGACTTCTCACTCTGAGCCTGGAGAGTGGGCT 1960			
GGGCCTGGACTCCTGAGACCTGGGAGCCTGACACCCCTCT 2000			
2010	2020	2030	2040
TCGGGTGCTTCTCCTGCCTGGCCACATGGACAGCAGCACC 2040			
TGTGAGAGTAGGAAAATGGAACCTGAGTGGCTGGGACCCC 2080			
TCTCCTACTTCCCACTATGCATCCATTTTGCTCTGCCTT 2120			
GATCTTTTTCTCCATCTCTTTTCTCCCTACCCAGCAGGAG 2160			
CCCCACAAACACATGTTGGCTGCTGTGCTCCTGCAGTTGGA 2200			
2210	2220	2230	2240
CCAGTGTCAGGGGTACAGGCTTCAGGCTGTGACCCACAC 2240			
TGGTACCCACCTCCCTTTCTTATTTTGCTTAGGTTTCATC 2280			
CACGGTTCCTCTGTGGAGCAAGTGGGGGCCACATAGCTG 2320			
CTGTCCCTGCTGAGGGTTGGTAGCAATCACACCCCTCATGT 2360			
CAGCTGGGAGACACGCGCAGTCTCCCACTGACCCCCAATC 2400			
2410	2420	2430	2440
AACTGAAATATTGTTTTGACTACTTTTTGTTTTTTTGT 2440			
TTTTTGTTTTTTTTTTTTTCGAGACAGAGTTCTCTGTA 2480			
TAGCCCTGGCTGTCTGGAACCTCACTTTGTAGACCAGGCT 2520			
GGCCTCGAACTCAAAAATCCTCCTGACTCTGCCTCTGCTT 2560			
CCCAAGTGCTGGGATTAAAGACGTGCGCCACCACCGCCTG 2600			

Fig. 42B

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mmFATP1 full length.DNA

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2610 2620 2630 2640

---

GCTGTTTTGTATTTTGTGTTTGTGACGATAGGGTCTC 2640  
ACTGTGGAGGCCAAGCTGGCCTCAGACTCCCCACCCATT 2680  
GCCTCTGGGCACCATTTCTATATTCTCAGACTGATGACAAT 2720  
GCACTAGTGTCCCTAGGAGTCTTGAGTCTGCACTTTCCCC 2760  
TCATAGCCTCAAGCTTCCAGAACTGACTCTGATCACTTGG 2800

---

2810 2820 2830 2840

---

ATGTGGCTAGTGTTGGCTCTACCCACATGTGTCAATTCAG 2840  
GGGTCCCCAGGCATAGTCTCTGGAAGCCCTCACCCGGAAA 2880  
AAGCTTGGAGAGACCCAGGAAGGTTGTTGTGTTCTTTGG 2920  
GCACCCCTGGTGGCAGTCTTGGGCATGCTTCCGCACTGT 2960  
ACTGGTGCATATAGCCAGACCTATGACATTTGAGGTCTA 3000

---

3010 3020 3030 3040

---

CCCTTCTGGCTCCTGTGGTCCCCATTGAGATCCTTGGTGA 3040  
CTCACCTCAGTCACCAAGCAGAGCCTCTGCCTGCCTTCAT 3080  
CTTCAAGGTCATGAAGGATGTGGACAGAGCAGCTACAGGC 3120  
TGCCAGCAGTCAACCACATGAGAGTGTTACTTCCTTGTG 3160  
GTTTTTAAAAAATAAATGTGCTGAGCCTCGAAAAAAAAAA 3200

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3210 3220 3230 3240

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AAAAAAAAAAAAAAAA 3217

Fig. 62C



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mmFATP1 full length.protein

```
      10      20      30      40
.....|.....|.....|.....|
MRAPGAGTASVASLALLWFLGLPWTWSAAAFCVYVGGGG 40
WRFLRIYCKTARRDLFGLSVLIRVRLELRRHRRAGDTIPC 80
IFOAVARRQPERLALVDASSGICWTFQAQLDTYSNAVANLF 120
RQLGFAPGDVVAVFLEGRPEFVGLWLGLAKAGVVAALLNV 160
NLRREPLAFCLGTSAAKALIYGGEMAAVAEVSEQLGKSL 200
      210      220      230      240
.....|.....|.....|.....|
LKFCSGDLGPESILPDTQLLDPMLAEAPTTPLAQAPGKGM 240
DDRIFYIYTSGETTGLPKAAIVVHSRYRRIAAFQHHSYSMR 280
AADVLYOCLPLYHSAGNIMGVGCQVIYGLTVVLRKKFSAS 320
RFWDDCVKYNCTVVDDIGEICRYLLROPVRDVEQRHRVRL 360
AVGNGLRPAIWEEFTORFGVPOIGEFYGATECNCSTIANMD 400
      410      420      430      440
.....|.....|.....|.....|
GKVGSCGFNSRILTHVYPIRLVKVNEDTMEPLRDSEGLCI 440
PCQPGEPGLLVGQINQQOPLRRFDGYVSDSATNKKIAHSV 480
FRKGD SAYLSGDVLYMDELGYMYFRDRSGDTFRWRGENVS 520
TTEVEAVLSRLLGQTDVAVYGVAVPGVEGKAGMAA!ADPH 560
SQLOPNSMYQELQKVLASYARPIFLRLLPQVDTTGTFKIQ 600
      610      620      630      640
.....|.....|.....|.....|
KTRLREGFDPROTSDRLEFFLDLKSGTRYLPDDEVHARI 640
CAGDFSL 647
```

Fig. 63

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mmFATP2 full length.DNA

```

      10      20      30      40
      |      |      |      |
GGGCGGAGGCCGAGCCAGTCGCCAGCTCCTGCTCTGCTC 40
CTCTCCCGCCTGCCGCCGCGCTGCAGGCCTCGAGCACTCC 80
CTCGGCCCCGGCGGGGACCGGGACCCCGCAGCTACCGCC 120
ATGCTGCCAGTGCTCTACACCGGCCTGGCGGGGCTGCTGC 160
TGCTGCCTCTGCTGCTCACCTGCTGCTGCCCCCTACCTCCT 200
      210      220      230      240
      |      |      |      |
CCAAGATGTGCGGTACTTCCTGCGGCTGGCCAACATGGCC 240
CGGCGGGTGCGCAGCTACCGGCAGCGGCGACCGTGCGTA 280
CCATCCTGCGGGCCTTCCTGGAACAAGCGCGCAAGACCCC 320
ACACAAGCCCTTCCTGCTGTTCCGAGACGAGACGCTCACC 360
TACGCCCAGGTGGACCGGCGCAGCAACCAAGTGGCGCGGG 400
      410      420      430      440
      |      |      |      |
CGCTGCACGATCAACTGGGCCTACGACAGGGGGATTGCGT 440
AGCCCTCTTCATGGGCAATGAGCCGGCCTACGTGTGGATC 480
TGGCTGGGACTGCTCAAACCTGGGCTGTCCCATGGCGTGCC 520
TCAACTACAACATTCTGTGCCAAGTCTCTGCTGCACTGCTT 560
TCAATGCTGCGGGGCGAAGGTGCTGCTGGCCTCCCCAGAT 600
      610      620      630      640
      |      |      |      |
CTACAAGAAGCTGTGGAGGAGGTTCTTCCAACCCTGAAAA 640
AGGATGCCGTGTCCGTCTTTTACGTAAGCAGAACTTCTAA 680
CACAAATGGTGTGGACACAATACTGGACAAAGTAGACGGA 720
GTGTGCGCGGAACCCACCCCGGAGTCGTGGAGGTCTGAAG 760
TCACTTTTACCACGCCAGCAGTATACATTTATAC TTCGGG 800
      810      820      830      840
      |      |      |      |
AACCACAGGTCTTCCAAAAAGCGGAACCATCAATCATCAT 840
CGCCTAAGGTATGGGACAAGCCTTGCTATGTCGAGTGGGA 880
ATCACGGCCAAGGATGTCATCTATACCAACAATGCCCTTG 920
TTCCAACAGTGCAACGCTCAAGATCGGCCTTCACGGATGC 960
ATCCTGGGTTGGGGCTACTTTAACCTTGGCGGGGCAAATT 1000
      1010      1020      1030      1040
      |      |      |      |
CTCAAGCAAGCCAATTTTGGGAACGACTGGCAGGAAATAC 1040
AACGTCAACGGTCATTTCAGTACATTGGTGAAGTGTTCGG 1080
TACCTGTGCAACACACCGCAGAAACCAATGACCGGGACC 1120
ACAAAGTGAAAAAAGCCCTGGGAAATGGCTTACGAGGAGA 1160
TGTGTGGAGAGAGTTCATCAAGAGATTTGGGGACATCCAC 1200

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Fig. 64A

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mmFATP2 full length.DNA

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1210      1220      1230      1240

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GTGTATGAGTTCTACGCATCCACTGAAGGCAACATTGGAT 1240  
TTGTGAACTATCCAAGGAAAATCGGTGCTGTGCGGAGAGC 1280  
AAACTACCTACAAAGAAAAGTTGCAAGGTATGAGCTGATC 1320  
AAGTATGACGTGGAGAAGGACGAGCCGGTCCGTGACGCAA 1360  
ATGGATATTGCATCAAAGTCCCCAAAGGTGAGGTTGGACT 1400

---

1410      1420      1430      1440

---

CTTGGTTTGCAAAATCACACAGCTCAACCATTTATTGGC 1440  
TATGCTGGAGGAAAAGACCCAGACAGAGAAGAAAAAACTCA 1480  
GAGATGTCTTTAAGAAAGGCGACATCTACTTCAACAGCGG 1520  
AGACCTCCTGATGATCGACCGTGAGAACTTCGTCTACTTT 1560  
CACGACAGGGTTGGAGATACTTTCCGGTGGAAAGGAGAGA 1600

---

1610      1620      1630      1640

---

ACGTAGCTACCACAGAAGTCGCTGACATCGTGGGACTGGT 1640  
AGATTTTGTGAAGAAGTGAATGTGTATGGCGTGCCTGTG 1680  
CCAGGTCATGAGGGTCTGAATTGGGATGGCCTCCCTCAAGA 1720  
TCAAAGAAAACACGAGTTCAATGGAAAGAACTCTTTCA 1760  
ACACATCGCGGAGTACCTGCCCAGTTACGCGAGGCCTCGG 1800

---

1810      1820      1830      1840

---

TTCTGAGGATACAAGATACCATTGAGATCACTGGGACTT 1840  
TTAAACACCGCAAAGTGACCCTGATGGAAGAGGGCTTCAA 1880  
TCCCACAGTCATCAAAGATACCTTGTATTTTCATGGATGAT 1920  
GCAGAGAAAACATTTGTGCCCATGACTGAGAACATTTATA 1960  
ATGCCATAATTGATAAAACTCTGAAGCTCTGAATATTCCC 2000

---

2010      2020      2030      2040

---

TGGTGGTTTAGCTCATGACATTTCCAGAAAGAACTCGAT 2040  
AGACCTCGCAGAGCCACTTCATACGTAGAATCCAACTTTA 2080  
ACTTGATTGAAGACTATAAGGTGCGATTTTATTTTATAGGA 2120  
AATTATTCATTAAAAGGATAGTTTTTTTTTTTTTTTTTAA 2160  
TTACACCTGAACCTTTGCAAGTAAAAAGATTTAGAGACAA 2200

---

2210      2220      2230      2240

---

TTATTTTTCAATGTGCACCTGCCATTTGTCCTTGCAAAC 2240  
AAGCTTCTTGGAGAGAGGGCCTTATTTTTTTAAAGACATA 2280  
ATAAACTATATTAACACTAAAAAATAAAAAAAAAAAAAA 2320  
AAAAAAAAAAAAAAAAAAAA 2338

Fig. 64B

mmFATP2 full length.protein

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10 20 30 40  
MLPVLTYGLAGLLLL PLLLLTCCCPYLLQDVRYFLRLANMA 40  
RRVRSYRORRPVRTILRAFLEOARKTPHKPFLLFRDETLT 80  
YAQVDRRSNOVARALHDQLGLROGDCVALFMGNEPAYVWI 120  
WLGLLKLGCPMACLNYNIRAKSLLHCFQCCGAKVLLASPD 160  
LOEAVEEVLP TLKKDAVS VFYVSRTSNTNGVDTILOKVDG 200  
210 220 230 240  
VSAEPTPESWRSEVTFTTPAVYIYTS GTTGLPKSGTINHH 240  
RLRYGTSLAMSSGNHGQGGCHLYQQCPCSNSATLKIGLHGC 280  
ILGWGYFNLGGANSOASQFWERLAGNTTSTVIOYIGELLR 320  
YLCNTPQKPNDRDHKVKKALGNGLRGDVWREFIKRFGDIH 360  
VYEFYASTEIGNIGFVNYPRKIGAVGRANYLORKVARYELI 400  
410 420 430 440  
KYDVEKDEPVRDANGYCIKVPKGEVGLLVCKITQLTPFIG 440  
YAGGKTOTEKKLRDVFKKGDIYFNSGDLLMIDRENFVYF 480  
HDRVGDTRFWKGENVATTEVADIVGLVDFVEEVNYYGVPV 520  
PGHEGRIGMASLKIKENYEFNGKKLFOHIAEYLP SYARPR 560  
FLRIQDTIEITGTFKHKRVTLMEEGFNPTVIKDTLYFMDD 600  
610 620 630 640  
AEKTFVPMTENIYNAIIDKTLKL. 624

Fig. 65

mmFATP3 partial.DNA

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10 20 30 40  
GAAAGCTCTGAGAGCGGGTGCAGTCTGGCCTGGCGTCTCG 40  
CGTACCTGGCCCGGGAGCAGCCGACACACACCTTCTCAT 80  
CCACGGCGCGCAGCGCTTTAGCTACGCGGAGGCTGAGCGC 120  
GAGAGCAACCGGATTGCTCGCGCCTTTCTGCGCGCACGGG 160  
GCTGGACCGGGGGCGCCGAGGCTCGGGCAGGGGCAGCAC 200

210 220 230 240  
TGAGGAAGGGCGACGCGTGGCGCCTCCGGCTGGAGATGCG 240  
GCTGCTAGAGGGACGACCGCGCCCCCTCTGGCACCCGGGG 280  
CGACCGTGGCGCTGCTCCTCCCAGCGGGCCCGGATTTCT 320  
TTGGATTTGGTTCGGACTGGCCAAAGCTGGCCTGCGCACG 360  
GCCTTTGTGCCACCGCTTTACGCCGAGGACCCCTGCTGC 400

410 420 430 440  
ACTGCCTCCGCAGCTGCGGTGCGAGTGGCTCGTGCTGGC 440  
CACAGAGTTCCTGGAGTCCCTGGAGCCGGACCTGCCGGCC 480  
TTGAGAGCCATGGGGCTCCACCTATGGGCGACGGGCCCTG 520  
AAACTAATGTAGCTGGAATCAGCAATTTGCTATCGGAAGC 560  
AGCAGACCAAGTGGAATGAGCCAGTGCCGGGGTACCTCTET 600

610 620 630 640  
GCCCCCAGAACATAATGGACACCTGCCTGTACATCTTCA 640  
CCTCTGGCACTACTGGCCTGCCAAGGCTGCTCGAATCAG 680  
TCATCTGAAGGTTCTACAGTGCCAGGGATTCTACCATCTG 720  
TGTGGAGTCCACCAGGAGGACGTGATCTACCTCGCACTCC 760  
CACTGTACCACATGTCTGGCTCCCTTCTGGGCATTGTGGG 800

810 820 830 840  
CTGCTTGGGCATTGGGGCCACCGTGGTGCTGAAACCCAAG 840  
TTCTCAGCTAGCCAGTTCTGGGACGATTGCCAGAAACACA 880  
GGGTGACAGTGTTCCAGTACATTGGGGAGTTGTGCCGATA 920  
CCTCGTCAACCAGCCCCGAGCAAGGCAGAGTTTGACCAT 960  
AAGGTGCGCTTGGCAGTGGGCAGTGGGTGCGCCCAGACA 1000

1010 1020 1030 1040  
CCTGGGAGCGTTTCTGCGGCGATTTGGACCTCTGCAGAT 1040  
ACTGGAGACGTATGGCATGACAGAGGGCAACGTAGCTACG 1080  
TTCAATTACACAGGACGGCAGGGTGCAGTGGGGCGAGCTT 1120  
CCTGGCTTTACAAGCACATCTTCCCTTCTCCTTGATTCTG 1160  
ATACGATGTCATGACAGGGGAGCCTATTCGGAATGCCCAG 1200

Fig. 66A

mmFATP3 partial.DNA 79/117

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1210 1220 1230 1240

GGGCACTGCATGACCACATCTCCAGGTGAGCCAGGCCTAC 1240  
TGGTGGCCCCAGTGAGCCAGCAGTCCCCCTTCTGGGCTA 1280  
TGCTGGGGCTCCGGAGCTGGCCAAGGACAAGCTGCTGAAG 1320  
GATGTCTTCTGGTCTGGGGACGTTTTCTTCAATACTGGGG 1360  
ACCTCTTGGTCTGTGATGAGCAAGGCTTCTTCACTTCCA 1400

---

1410 1420 1430 1440

CGATCGTACTGGAGACACCATCAGGTGGAAGGGAGAGAAT 1440  
GTGGCCACAACCTGAAGTGGCTGAGGTCTTGGAGACCCTGG 1480  
ACTTCTTTCAGGAGGTGAACATCTATGGAGTCACGGTGCC 1520  
AGGGCACGAAGGCAGGGCAGGCATGGCGGCCTTGGCTCTG 1560  
CGGCCCCCGCAGGCTCTGAACCTGGTGCAGCTCTACAGCC 1600

---

1610 1620 1630 1640

ATGTTTCTGAGAACTTGCCACCGTATGCCCGACCTCGGTT 1640  
TCTCAGGCTCCAGGAATCTTTGGCCACTACTGAGACCTTC 1680  
AAACAGCAGAAGGTTAGGATGGCCAATGAGGGCTTTGACC 1720  
CCAGTGTACTGTCTGACCCACTCTATGTTCTGGACCAAGA 1760  
TATAGGGGCCTACCTGCCCCCTCACACCTGCCCGGTACAGT 1800

---

1810 1820 1830 1840

GCCCTCCTGTCTGGAGACCTTCGAATCTGAAACCTTCCAC 1840  
TTGAGGGAGGGGCTCGGAGGGTACAGGCCACCATGGCTGC 1880  
ACCAGGGAGGGTTTTTCGGGTATCTTTGTATATGGAGTCA 1920  
TTATTTTGTAAATAAACAGCTGGAGCTTAAAAAAAAAAAAA 1960  
AAA 1998

Fig. 66B

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mmFATP3 partial.protein

10 20 30 40  
ESSESGCSLAWRLAYLAREOPTHTFLIHGAORFSYAEER 40  
ESNRIARAFLRARGWTGGRRGSGRGSTEEGARVAPPAGDA 80  
AARGTTAPPLAPGATVALLLPAGPDFLWIWFGGLAKAGLRT 120  
AFVPTALRRGPLLHCLRSCGASALVLA TEFLSLEPDLPA 160  
LRAMGLHLWATGPETNVAGISNLLSEAADOVDEPVPGYLS 200  
210 220 230 240  
APQIMDTCLYIFTSGTTGLPKAARISHLKVLQCGFYHL 240  
CGVHQEDVIYLALPLYHMSGSLLGIVGCLGIGATVVLKPK 280  
FSASQFWDCCQKHRVTVFQYIGELCRYLVNOPPSKAEFDH 320  
KVR LAVGSGLRPD TWERFLRRFGPLQILETYGMTEGNVAT 360  
FNYTGRQGA VGRASWLYKHIFPFSLIRYDVM TGEP I RNAQ 400  
410 420 430 440  
GHCMTTSPGEPGLLVAPVSQOSPFLGYAGAPELAKDKLLK 440  
DVFWSGDVFFNTGOLLVCDEQGFLHFHRTGDTIRWKGEN 480  
VATTEVAEVLETLDLFLOEVNIYGVTVP GHEGRAGMAALAL 520  
RPPQALNLVQLYSHVSENLPYARPRFLRLQESLATTETF 560  
KQKQVRMANEGFDPSVLS DPLYVLDQD IGAYLPLTPARYS 600  
610 620 630 640  
ALLSGDLRI. 610

Fig. 67

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mmFATP4 full length.DNA

10 20 30 40  
ATGCTGCTTGGAGCCTCTCTGGTGGGGGCGCTACTGTTCT 40  
CCAAGCTAGTGCTGAAGCTGCCCTGGACCCAGGTGGGATT 80  
CTCCCTGTTGCTCCTGTACTTGGGGTCTGGTGGCTGGCGT 120  
TTCATCCGGGTCTTCATCAAGACGGTCAGGAGAGATATCT 160  
TTGGTGGCATGGTGCTCCTGAAGGTGAAGACCAAGGTGCG 200  
210 220 230 240  
ACGGTACCTTCAGGAGCGGAAGACGGTGCCCTGCTGTTT 240  
GCTTCAATGGTACAGCGCCACCCGGACAAGACAGCCCTGA 280  
TTTTCGAGGGCACAGACACTCACTGGACCTTCGCCAGCT 320  
GGATGAGTACTCCAGTAGTGTGGCCAACCTCCTGCAGGCC 360  
CGGGGCTGGCCTCAGGCAATGTAGTTGCCCTCTTTATGG 400  
410 420 430 440  
AAAACCGCAATGAGTTTGTGGGTCTGTGGCTAGGCATGGC 440  
CAAGCTGGGCGTGGAGGGCGGTCTCATCAACACCAACCTT 480  
AGGCGGGATGCCCTGCGCCACTGTCTTGACACCTCAAAGG 520  
CACGAGCTCTCATCTTTGGCAGTGAGATGGCCTCAGCTAT 560  
CTGTGAGATCCATGCTAGCCTGGAGCCACACTCAGCCTC 600  
610 620 630 640  
TTCGTCTCTGGATCCTGGGAGCCCAGCACAGTGCCCGTCA 640  
GCACAGAGCATCTGGACCTCTTCTGGAAGATGCCCGGAA 680  
GCACCTGCCCAGTCACCCAGACAAGGGTTTTACAGATAAG 720  
CTCTTCTACATCTACACATCGGGCACCACGGGGCTACCCA 760  
AAGCTGCCATTGTGGTGCACAGCAGGTATTATCGTATGGC 800  
810 820 830 840  
TTCCCTGGTGTACTATGGATTCGCGATGCGGCCTGATGAC 840  
ATTGTCTATGACTGCCTCCGCCCTTACCACTCAAGCAGGA 880  
AACATCGTGGGGATTGGCAGTGCTTACTCCACGGCATGAC 920  
TGTGGTGTCCGGAAGAAGTTCAGCCTCCCGGTTCTGG 960  
GATGATTGTATCAAGTACAACCTGCACAGTGGTACAGTACA 1000  
1010 1020 1030 1040  
TTGGCGAGCTCTGCCGCTACCTCCTGAACCAGCCACCCCG 1040  
TGAGGCTGAGTCTCGGCACAAGGTGCGCATGGCACTGGGC 1080  
AACGGTCTCCGGCAGTCCATCTGGACCGACTTCTCCAGCC 1120  
GTTTCCACATCCCCCAGGTGGCTGAGTTCTATGGGGCCAC 1160  
TGAATGCAACTGTAGCCTGGGCAACTTTGACAGCCGGGTG 1200

Fig. 68A



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## mmFATP4 full length.DNA

```
      1210      1220      1230      1240
      +-----+-----+-----+-----+
GGGGCCTGTGGCTTCAATAGCCGCATCCTGTCCTTTGTGT 1240
ACCTATCCGTTTGGTACGTGTCAATGAGGATACCATGGA 1280
ACTGATCCGGGGACCCGATGGAGTCTGCATTCCCTGTCAA 1320
CCAGGTGAGCCAGGCCAGCTGGTGGGTCGCATCATCCAGC 1360
AGGACCCCTGCGCCGTTTCGACGGGTACCTCAACCAGGG 1400

      1410      1420      1430      1440
      +-----+-----+-----+-----+
TGCCAACAACAAGAAGATTGCTAATGATGTCTTCAAGAAG 1440
GGGGACCAAGCCTACCTCACTGGTGACGTCTGGTGATGG 1480
ATGAGCTGGGTTACCTGTACTTCCGAGATCGCACTGGGGA 1520
CACGTTCCGCTGGAAAGGGGAGAATGTATCTACCACTGAG 1560
GTGGAGGGGCACACTCAGCCGCTGCTTCATATGGCAGATG 1600

      1610      1620      1630      1640
      +-----+-----+-----+-----+
TGGCAGTTTATGGTGTTGAGGTGCCAGGAAGTGAAGGCCG 1640
AGCAGGAATGGCTGCCGTTGCAAGTCCCATCAGCAACTGT 1680
GACCTGGAGAGCTTTGCACAGACCTTGAAAAAGGAGCTGC 1720
CTCTGTATGCCCCGCCCATCTTCCTGCGCTTCTTGCCTGA 1760
GCTGCACAAGACAGGGACCTTCAAGTTCAGAAAGACAGAG 1800

      1810      1820      1830      1840
      +-----+-----+-----+-----+
TTGCGGAAGGAGGGCTTTGACCCATCTGTTGTGAAAGACC 1840
CGCTGTTCTATCTGGATGCTCGGAAGGGCTGCTACGTTGC 1880
ACTGGACCAGGAGGCTTATACCGCATCCAGGCAGGCGAG 1920
GAGAAGCTGTGATTTCCCTTACATCCCTCTGAGGGCCAG 1960
AAGATGCTGGATTGAGAGCCCTAGCGTCCACCCAGAGGG 2000

      2010      2020      2030      2040
      +-----+-----+-----+-----+
TCCTGGGCAATGCCAGACCAAAGCTAGCAGGGCCCCGCACC 2040
TCCGCCCCCTAGGTGCTGATCTCCCTCTCCCAAAGTCCA 2080
AGTGACTCACTGCCGCTTCCCCGACCTCCAGAGGCTTTC 2120
TGTGAAAGTCTCATCAAGCTGTGTCTTCTGGTCCAGGCG 2160
TGGCCCCCTGGCCCCAGGGTTTCTGATAGGCTCCTTTAGGA 2200

      2210      2220      2230      2240
      +-----+-----+-----+-----+
TGGTATCTTGGGTCCAGCGGGCCAGGGTGTGGGAGAGGAG 2240
TCACTAAGATCCCTCCAATCAGAAGGGAGCTTACAAAGGA 2280
ACCAAGGCAAAGCCTGTAGACTCAGGAAGCTAAGTGGCCA 2320
GAGACTATAGTGGCCAGTCATCCCATGTCCACAGAGGATC 2360
TTGGTCCAGAGCTGCCAAAGTGTACCTCTCCCTGCCTGC 2400

      2410      2420      2430      2440
      +-----+-----+-----+-----+
ACCTCTGGGGAAAAGAGGACAGCATGTGGCCACTGGGCAC 2440
CTGTCTCAAGAAGTCAGGATCACACACTCAGTCCTTGTTT 2480
CTCCAGGTTCCCTTGTCTTGTCTCGGGGAGGGAGGGACG 2520
AGTGCTCTGTCTGTCTTCTGCTGCTGTGAGTCTGTG 2560
TTGCTTCTCCATCTGTCTAGCCTGAGTGTGGGTGGAACA 2600
```

Fig. 68B

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mmFATP4 full length.DNA

2610 2620 2630 2640

GGCATGAGGAGAGTGTGGCTCAGGGGCCAATAAACTCTGC 2640

CTTGACTCCTCTTAAAAAAAAAAAAAAAAAAAAAAAAAAAA 2680

AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA 2710

Fig. 68C

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mmFATP4 full length.protein

10 20 30 40  
MLLGASLVGALLFSKLVKLKPWTQVGFSLLLLYLGSGGWR 40  
FIRVFIKTVRRDIFGGMVLLKVTKVRRYLQERKTVPLLF 80  
ASHVQRHPDKTALIFEGTDTHWTFRQLDEYSSSVANFLQA 120  
RGLASGNVVALFMENRNEFVGLWLGMALGVEAALINTNL 160  
RRDALRHCLDTSKARALIFGSEMASAICEIHASLEPTLSL 200  
210 220 230 240  
FCSGSWEPSTVPVSTEHLOPILLEDAPKHLPSHPDKGFTDK 240  
LFYIYTSGTTGLPKAAIVVHSRYRMASLVYYGFRMRPD 280  
IYYDCLPLYHSSRKHRGOWQCLLHGMTVVIRKKFSASRFW 320  
DDCIKYNCTVVQYIGELCRYLLNOPPREAESRHKVARMALG 360  
NGLRQSIWTFSSRFHIPQVAEFYGATECNCSLGNFDSRV 400  
410 420 430 440  
GACGFNSRILSFVYPIRLVVRVNEDTMELIRGPDGVCIPCQ 440  
PGQPGQLVGRIIQQDPLRRFDGYLNQGANNKKIANDVFKK 480  
GDQAYLTGOVLVMOELGYLYFRDRTGOTFRWKGENVSTTE 520  
VEGTLRLLHMADVAVYGVEVPGTEGRAGMAAVASPI SINC 560  
DLESFAQTLKKELPLYARPIFLRFLPELHKTGTGFKFQKTE 600  
610 620 630 640  
LRKEGFDPSVVKDPLFYLDARKGCYVALDQEA YTRIOAGE 640  
EKL. 644

Fig. 69

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mmFATPS full length.DNA

```
      10      20      30      40
+-----+
CACTCATCAGAGCTAAGAGAGACTACACGCTCTCATCTAC 40
TTCAGAAAGAGCCAATGCCATGGGTATTTGGAAGAACTA 80
ACCTTACTGCTGTTGCTGCTTCTGCTGGTTGGCCTGGGGC 120
AGCCCCCATGGCCAGCAGCTATGGCTCTGGCCCTGCGTTG 160
GTTCTGGGAGACCCACATGCCTTGTGCTGCTTGGCTTG 200
      210      220      230      240
+-----+
GCATTGCTGGGCAGACCCTGGATCAGCTCCTGGATGCCCC 240
ACTGGCTGAGCCTGGTAGGAGCAGCTCTTACCTTATTCCT 280
ATTGCCTCTACAGCCACCCCCAGGGCTACGCTGGCTGCAT 320
AAAGATGTGGCTTTCACCTTCAAGATGCTTTTCTATGGCC 360
TAAAGTTCAGGCGACGCCTTAACAAACATCCTCCAGAGAC 400
      410      420      430      440
+-----+
CTTTGTGGATGCTTTAGAGCGGCAAGCACTGGCATGGCCT 440
GACCGGGTGGCCTTGGTGTGTACTGGGTCTGAGGGCTCCT 480
CAATCACAAATAGCCAGCTGGATGCCAGGTCCTGTCAAGC 520
AGCATGGGTCTGAAAGCAAAGCTGAAGGATGCCGTAATC 560
CAGAACACAAGAGATGCTGCTGCTATCTTAGTTCTCCCGT 600
      610      620      630      640
+-----+
CCAAGACCATTTCTGCTTTGAGTGTGTTTCTGGGGTTGGC 640
CAAGTTGGGCTGCCCTGTGGCCTGGATCAATCCACACAGC 680
CGAGGGATGCCCTTGCTACACTCTGTACGGAGCTCTGGGG 720
CCAGTGTGCTGATTGTGGATCCAGACCTCCAGGAGAACCT 760
GGAAGAAGTCCTTCCCAAGCTGCTAGCTGAGAACATTAC 800
      810      820      830      840
+-----+
TGCTTCTACCTTGGCCACAGCTCACCCACCCCGGGAGTAG 840
AGGCTCTGGGAGCTTCCCTGGATGCTGCACCTTCTGACCC 880
AGTACCTGCCAGCCTTCGAGCTACGATTAAGTGGAAATCT 920
CCTGCCATATTCATCTTTACTTCAGGGACCACTGGACTCC 960
CAAAGCCAGCCATCTTATCACATGAGCGGGTCATACAAGT 1000
      1010      1020      1030      1040
+-----+
GAGCAACGTGCTGTCTTCTGTGGATGCAGAGCTGATGAT 1040
GTGGTCTATGACGTCCCTACCTCTGTACCATACGATAGGGC 1080
TTGTCTTGGATTCCCTTGGCTGCTTACAAGTTGGAGCCAC 1120
CTGTGTCTGGCCCCCAAGTTCTCTGCCTCCCGATTCTGG 1160
GCTGAGTGCCGGCAGCATGGCGTAACAGTGATCTTGTATG 1200
```

Fig. 70A

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mmFATP5 full length.DNA

```
      1210      1220      1230      1240
TGGGTGAAATCCTGCGGTACTTGTGTAACTCCCTGAGCA 1240
ACCAGAAGACAAGATACATACAGTGGCTTGGCCATGGGA 1280
ACTGGACTTCGGGCAAATGTGTGGAAAACTTCCAGCAAC 1320
GCTTTGGTCCCATTCGGATCTGGGAATTCTACGGATCCAC 1360
AGAGGGCAATGTGGGCTTAATGAACTATGTGGGCCACTGC 1400
      1410      1420      1430      1440
GGGGCTGTGGGAAGGACCAGCTGCATCCTTCGAATGCTGA 1440
CTCCCTTTGAGCTTGTACAGTTTCGACATAGAGACAGCAGA 1480
GCCTCTGAGGGACAAACAGGGTTTTTGCATTCTGTGGAG 1520
CCAGGAAAGCCAGGACTTCTTTTGACCAAGGTTGAAAAGA 1560
ACCAACCTTCCCTGGGCTACCGTGGTTCCAGGCCGAGTC 1600
      1610      1620      1630      1640
CAATCGGAAACTTGTTCGAATGTACGACGCGTAGGAGAC 1640
CTGTACTTCAACACTGGGGACGTGCTGACCTTGGACCAGG 1680
AAGGCTTCTTCTACTTTCAAGACCGCCTTGGTGACACCTT 1720
CCGGTGGAAAGGGCGAAAACGTATCTACTGGAGAGGTGGAG 1760
TGTGTTTTGTCTAGCCTAGACTTCCTAGAGGAAGTCAATG 1800
      1810      1820      1830      1840
TCTATGGTGTGCTGTGCCAGGGTGTGAGGGTAAGGTTGG 1840
CATGGCTGCTGTGAAACTGGCTCCTGGGAAGACTTTTGAT 1880
GGGCAGAAGCTATACCAGCATGTCCGCTCCTGGCTCCCTG 1920
CCTATGCCACACCTCATTTTCATCGGTATCCAGGATTCCCT 1960
GGAGATCACAAACACCTACAAGCTGGTAAAGTCACGGCTG 2000
      2010      2020      2030      2040
GTGCGTGAGGGTTTTGATGTGGGGATCATTGCTGACCCCC 2040
TCTACATACTGGACAACAAGGCCAGACCTTCCGGAGTCT 2080
GATGCCAGATGTGTACCAGGCTGTGTGTGAAGGAACCTGG 2120
AATCTCTGACCACCTAGCCAACTGGAAGGCAATCCAAAAG 2160
TGTAAGAGATTGACACTAGTCAGCTTCACAAAGTTGTCCGG 2200
      2210      2220      2230      2240
GTTCCAGATGCCCATGGCCCAGTAGTACTTAGAGAATAAA 2240
CTTGAATGTGTATACAAAAAAAAAAAAAAAAAAAAAAAA 2277
```

Fig. 70B

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mmFATP5 full length protein

10 20 30 40  
MGIWKKLTLLLLLLLLLVGLGQPPWPAAMALALRWFLGDPT 40  
CLVLLGLALLGRPWISSWMPHWLSLVGAALTFLPLQPP 80  
PGLRWLHKDVAFTFKMLFYGLKFRRRLNKHPPETFVDALE 120  
RQALAWPDRVALVCTGSEGSSITNSQLDARSCQAAWVLA 160  
KLKDAVIONTRDAAAIVLPSKITISALSVFLGLAKLGCPV 200  
210 220 230 240  
AWINPHSRGMPLLSVRSSGASVLI VOPDLQENLEEVLPAK 240  
LLAENIHCFYLGHSSTPGVEALGASLDAAPSDVPASLR 280  
ATIKWKSPAIFIFTSGTTGLPKPAILSHERVIQVSNVLSF 320  
CGCRADDVVYDVLPLYHTIGLVGLGFLGCLQVGATCVLAPK 360  
FSASRFWAECROHGVTVILYVGEILRYLCNVPEQPEDKIH 400  
410 420 430 440  
TVRLAMGTGLRANVWKNFQORFGPIRIWEFYGSTEGNVGL 440  
MNYVGHCGAVGRTSCILRMLTPFELVQFDIETAEPLRDKQ 480  
GFCIPVEPGKPGLLLTQVRKNOPFLGYRGSQAESNRKLVA 520  
NVRRVGDLYFNTGDVLTLDQEGFFYFQDRLGDTFRWKGEN 560  
VSTGEVECVLSSLOFLEEENVYGVVPGCEGKVGMAAVKL 600  
610 620 630 640  
APGKTFDGQKLYQHVRSWLPAYATPHFIRIQDSLEITNTY 640  
KLVKSRLLVREGFDVGIADPLYILDNKAOTFRSLMPDVYQ 680  
AVCEGTWNL 690

Fig. 71

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dmFATP partial.DNA

10 20 30 40  
GCTCTCTGGGCCTATATCAAGCTGCTGAGGTACACGAAGC 40  
GCCATGAGCGGCTCAACTACACGGTGGCGGACGTCTTCGA 80  
ACGAAATGTTTCAGGCCCATCCGGACAAGGTGGCTGTGGTC 120  
AGTGAGACGCAACGCTGGACCTTCCGTGAGGTGAACGAGC 160  
ATGCGAACAAAGGTGGCCAATGTGCTGCAGGCTCAGGGCTA 200

210 220 230 240  
CAAAAAGGGCGATGTGGTGGCCCTGTTGCTGGAGAACC GC 240  
GCCGAGTACGTGGCCACCTGGCTGGGTCTCTCCAAGATCG 280  
GTGTGATCACACCGCTGATCAACACGAATCTGCGCGGTCC 320  
CTCCCTGCTGCACAGCATCACGGTGGCCCATTTGCTCGGCT 360  
CTCATTTACGGCGAGGACTTCCTGGAAGCTGTCACCGACG 400

410 420 430 440  
TGGCCAAGGATCTGCCAGCGAACCTCACACTCTTCCAGTT 440  
CAACAACGAGAACAAACAACAGCGAGACGGAAAAGAACATA 480  
CCGCAGGCCAAGAATCTGAACGCGCTGCTGACCACGGCCA 520  
GCTATGAGAAGCCTAACAAAGACGCAGGTTAACCACCACGA 560  
CAAGCTGGTCTACATCTACACCTCCGGCACCACAGGATTG 600

610 620 630 640  
CCAAAGGCTGCGGTTATCTCTCACTCCCGTTATCTGTTTA 640  
TCGCTGCTGGCATCCACTACACCATGGGTTTCCAGGAGGA 680  
GGACATCTTCTACACGCCCTTGCCTTTGTACCACACCGCT 720  
GGTGGCATTATGTGCATGGGTGAGTCGGTGCTCTTTGGCT 760  
CCACGGTCTCCATTGCGAAGAAGTTCTCGGCATCCAATA 800

810 820 830 840  
TTTCGCGGACTGCGCCAAGTATAATGCAACTATTGGTCAG 840  
TATATCGGTGAGATGGCTCGCTACATTCTAGCTACGAAAC 880  
CCTCGGAATACGACCAGAAACACCGAGTGCGTCTGGTCTT 920  
TGGAAACGGACTGCGACCGCAGATTTGGCCACAGTTTGTG 960  
CAGCGCTTCAACATTGCCAAGGTTGGCGAGTTCTACGGCG 1000

1010 1020 1030 1040  
CCACCGAGGGTAATGCGAACATCATGAATCATGACAACAC 1040  
GGTGGGCGCCATCGGCTTTGTGTCGCGCATCCTGCCCAAG 1080  
ATCTACCCAATCTCGATCATTCGCGCCGATCCGGACACCG 1120  
GAGAGCCCATTAGAGATAGGAATGGCCTATGCCAACTGTG 1160  
CGCTCCCAACGAGCCAGGCGTATTCATCGGCAAGATCGTC 1200

Fig. 72A

dmFATP partial.DNA 89/117

1210 1220 1230 1240

AAAGGAAATCCTTCTCGCGAATTCCTCGGATACGTCGATG 1240  
AAAAGGCCCTCCGCGAAGAAGATTGTTAAGGATGTGTTCAA 1280  
GCATGGCGATATGGCTTTCATCTCCGGAGATCTGCTGGTT 1320  
GCCGACGAGAAGGGTTATCTGTACTTCAAGGATCGCACCG 1360  
GTGACACCTTCCGCTGGAAGGGCGAGAATGTTTCCACCAG 1400

1410 1420 1430 1440

CGAGGTGGAGGCGCAAGTCAGCAATGTGGCCGGTTACAAG 1440  
GATACCGTCGTTTACGGCGTAACCATTCGCGACACCGAGG 1480  
GAAGGGCCGGCATGGCCGCCATCTATGATCCGGAGCGAGA 1520  
ATTGGACCTCGACGTCTTCGCCGCTAGCTTGGCCAAGGTG 1560  
CTGCCCCGCTACGCTCGTCCCCAGATCATTGATTGCTCA 1600

1610 1620 1630 1640

CCAAGGTGGACCTGACTGGAACCTTTAAGCTGCGCAAGGT 1640  
AGACCTGCAGAAGGAGGGCTACGATCCGAACGCGATCAAG 1680  
GACGCGCTGTACTACCAGACTTCCAAGGGTCGGTACGAGC 1720  
TGCTCACGCCCCAGGTTTACGACCAGGTGCAGCGCAACGA 1760  
AATCCGCTTCTAAGAGCTGCAATAGAGTTGTGTCTGAACC 1800

1810 1820 1830 1840

TTGCCTTTTGCCCAATATGCTGTTAATTAGTTTGTAAGGC 1840  
TAAGTGTAGTAGAGGAAAATCGGGGGAAATCGGCAGCAAA 1880  
GATCATTCAGCCTAGGAGAGATGCATCCGAAGCACATTTT 1920  
CATGTCAACAATGCACTTTTGTATATCGTAAGCATATATA 1960  
TATCGTATATCGTAAACGTAGTTGTATCTGCATTTGTGTA 2000

2010 2020 2030 2040

GATGATAGCCTCCTATACGCATTTCAATTGTTTTTAGCGT 2040  
GCTAAAGAACCCTTGTTAAATGCAATTTAGCTATTGTTTA 2080  
GTCAGTTTTAGTGGCATTTACACTTCCATTCTCGTTGCGT 2120  
TTCGTTTTTGCTGTACATATGAGAAGCTCTGATGTTTTT 2160  
GTATCAAATAAAGTTTTTTCCTTCACCACGGACCACGTGA 2200

2210 2220 2230 2240

AAAAAAAAAAAAAAAAAAAAA 2221

Fig. 72B



dmFATP partial.protein

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10 20 30 40  
ALWAYIKLLRYTKRHERLNYTVADVFERNVQAHDPKVAVV 40  
SETORWTFROVNEHANKVANVLQAQGYKKGOVVALLENR 80  
AEYVATWLGSLKIGVITPLINTNLRGPSLLHSITVAHCSA 120  
LIYGEDFLEAVTDVAKDLPANLTLFOFNNNNNNSETEKNI 160  
POAKNLNALLTTASYEKPNTQVNHHDKLVIYITSGTTGL 200  
210 220 230 240  
PKAAVISHSRYLFAAGIHYTMGFQEEIDFYTPLPLYHTA 240  
GGIMCMQOSVLFGSTVSIRKKFSASNYFADCAKYNATIGQ 280  
YIGEMARYILATKPSEYDQKHRVRLVFGNLRPQIWPQFV 320  
QRFNIAKVGEFYGATEGNANIMNHONTVGAIGFVSRILPK 360  
IYPISIIIRADPDTGEPIRDRNGLCQLCAPNEPGVFIGKIV 400  
410 420 430 440  
KGNPSREFLGYYDEKASAKKIVKDVFKHGDMAFISGOLLV 440  
ADEKGYLYFKDRTGDTFRWKGENVSTSEVEAQVSNVAGYK 480  
DTVVYGVITPHTEGRAGMAAIYDPERELDLVFAASLAKV 520  
LPAYARPOIIRLLTKVDLTGTFKLRKVDLQKEGYDPNAIK 560  
DALYYQTSKGRYELLTPQVYDQVQRNEIRF 590

Fig. 73

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drFATP partial.DNA

10 20 30 40

---

AGTGTAGATACCACAGGAACGTTTAAAAATCCAGAAGACCA 40  
GACTGCAAAGGGAAGGATACGATCCACGGCTCACAACTGA 80  
CCAGATCTACTTCCTAAACTCCAGAGCAGGGCGTTACGAG 120  
CTTGTCAACGAGGAGCTGTACAATGCATTTGAACAAGGGC 160  
AGGATTTCCCTTT 173

*Fig. 74*

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drFATP partial.protein

10 20 30 40  
SVDTTGTFKIQKTRLOREGYDPRLTTDQIYFLNSRAGRYE 40  
LVNEELYNAFEQGQDFP 57'

*Fig. 75*

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ceFATPa coding only.DNA

```

      10      20      30      40
      |      |      |      |
ATGAAGCTGGAGGAGCTTGTGACAGTTATGCTTCTCACAG 40
TGGCTGTCATTGCTCAGAATCTCCGATTGGAGTAATATT 80
GGCTGGAGTTCTTATTTTATACATCACAGTGGTTCATGGA 120
GATTTCAATTATAGAAGTTATCTTACGTTGAATAGGGATT 160
TAACAGGATTGGCTCTAATTATTGAAGTCAAAATCGACCT 200
      210      220      230      240
      |      |      |      |
ATGGTGGAGGTTGCATCAGAATAAAGGAATCCATGAACTG 240
TTTTTGGATATTGTGAAAAAGAATCCAAATAAGCCGGCGA 280
TGATTGACATCGAGACGAATACAACAGAAACATACGCAGA 320
GTTCAATGCACATTGTAATAGATATGCCAATTATTTCCAG 360
GGTCTTGCTATCGATCCGGAGACGTTGTCGCCTTGTA 400
      410      420      430      440
      |      |      |      |
TGGAGAACTCGGTCGAGTTTGTGGCCGCGTGGATGGGACT 440
CGCAAAAATCGGAGTTGTAAACGGCTTGGATCAACTCGAAT 480
TTGAAAAGAGAGCAACTTGTTTCATTGTATCACTGCGAGCA 520
AGACAAAGGCGATTATCACAAGTGTAACACTTCAGAATAT 560
TATGCTTGATGCTATCGATCAGAAGCTGTTTGATGTTGAG 600
      610      620      630      640
      |      |      |      |
GGAATTGAGGTTTACTCTGTGCGGAGAGCCCAAGAAGAATT 640
CTGGATTCAAGAATCTCAAGAAGAAGTTGGATGCTCAAAT 680
TACTACGGAACCAAGACCCTTGACATAGTAGATTTTAAA 720
AGTATTCTTTGCTTCATCTATACAAGTGGTACTACTGGAA 760
TGCCAAAAGCCGCTGTCATGAAGCACTTCAGATATTACTC 800
      810      820      830      840
      |      |      |      |
GATTGCCGTTGGAGCCGCAAAATCATTGGAATCCGCCCT 840
TCTGATCGTATGTACGTCTCGATGCCAATTTATCACACTG 880
CAGCTGGAATTCTTGGAGTTGGGCAAGCTCTGTTGGGTGG 920
ATCATCGTGTGTCATTAGAAAAAAATTCTCGGCTAGCAAC 960
TTTTGGAGGGATTGTGTAAAGTATGATTGTACAGTTTCAC 1000
      1010      1020      1030      1040
      |      |      |      |
AATACATTGGAGAGATTTGTCGGTACTTGTTGGCTCAGCC 1040
AGTTGTGGAAGAGGAATCCAGGCATAGAATGAGATTGTTG 1080
GTTGGAACGGACTCCGTGCTGAAATCTGGCAACCATTTG 1120
TAGATCGATTCCGTGTCAGAATTGGAGAACTTTATGGTTC 1160
AACTGAAGGAACTTCATCTCTCGTGAACATTGACGGACAT 1200

```

Fig. 76A

Fig. 76B

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ceFATPa coding only.protein

10 20 30 40  
MKLEELVTVMLLTVAVIAQNLPVILAGVLIYITVVHG 40  
DFIYRSYLTNRDLTGLALIEVKIDLWRLHQNKGIEL 80  
FLDIVKKNPNKPAMIDIE TTTETYAEFNAHCNRYANYFO 120  
GLGYRSGDVVALYMENSVEFVAAWMGLAKIGVVTAWINSN 160  
LKREQLVHCITASKTKAII TSVTLQNI MLDAIDQKLFOVE 200

210 220 230 240  
GIEVYSVGEPKKNSGFKNLKKKLD AQTTEPKTLDIVDFK 240  
SILCFIYTSGTTGMPKAAVMKHFRYYSI AVGAAKSFGIRP 280  
SDRMVVSMP IYHTAAGILGVGOALLGGSSCVIRKKFSASN 320  
FWRDCVKYDCTVSQYIGE ICRYLLAQP VVEEESRHRMRL 360  
VGNGLRAE IWQPFVDRFRVRIGELYGSTEGTSSLVNIDGH 400

410 420 430 440  
VGACGFLPISPLTKKMHPVRLIKVDDVTGEAIRTSDGLCI 440  
ACNPGESGAMVSTIRKNNPLLQFEGYLNKKETNKKIIRDV 480  
FAKGDSCFLTGDLLHWDR LGYVYFKDRTGDTFRWKGENVS 520  
TTEVEAILHPITGLSDATVYGVEVPQREGRVGMASVVRVV 560  
SHEEDETQFVHRVGARLASSLT SYAIPQFMRICTQDVEKTG 600

610 620 630 640  
TFKLVKTNLQRLGIMDAPSDSIYIYNSENRNFVPFONDRL 640  
CKVSLGSYPF. 651

Fig. 77

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ceFATPb coding only.DNA

```

      10      20      30      40
      +-----+
ATGAGGGAAATGCCGGACAGTCCCAAGTTTGCGTTAGTCA 40
CGTTTGTGTGTATGCAGTGGTTTTGTACAATGTCAACAG 80
CGTTTTCTGGAAATTTGTATTCATCGGATATGTTGTTTT 120
AGGCTGCTTCGCACTGATTTTGAAGAAGAGCACTTGCCA 160
CGTTACCTAGAGATTTTGCGGGACTGAAGCTCTTAATATC 200
      210      220      230      240
      +-----+
GGTTAAGTCGACAATTCGTGGCTTGTTCAAGAAAGATCGC 240
CCAATTCATGAAATCTTTTGAATCAGGTGAAACAGCATC 280
CAAACAAAGTGCGGATTATTGAAATTGAAAGTGGTAGGCA 320
GTTGACGTATCAAGAATTGAATGCGTTAGCTAATCAGTAT 360
GCTAACCTTTACGTGAGTGAAGGTTACAAAATGGGCGACG 400
      410      420      430      440
      +-----+
TTGTCGCTTTGTTTATGGAAAATAGCATCGACTTCTTTGC 440
AATTTGGCTGGGACTTTCCAAGATTGGAGTCGTGTGCGGC 480
TTCATCAACTCAAACCTTGAAGTTGGAGCCATTGGCACATT 520
CGATTAATGTTTTCGAAGTGCAAATCATGCATTACCAATAT 560
CAATCTGTTGCCGATGTTCAAAGCCGCTCGTGAAAAGAAT 600
      610      620      630      640
      +-----+
CTGATCAGTGACGAGATCCACGTGTTTCTGGCTGGAATC 640
AGGTTGATGGACGTCATAGAAGTCTTCAGCAAGATCTCCA 680
TCTTTTCTCTGAGGATGAACCTCCAGTTATAGACGGACTC 720
AATTTTAGAAGCGTTCTGTGTTATATTTACACTTCCGGTA 760
CTACCGGAAATCCAAAGCCAGCCGTCATTAAACACTTCCG 800
      810      820      830      840
      +-----+
TTACTTCTGGATTGCGATGGGAGCAGGAAAAGCATTTGGA 840
ATTAATAAGTCAGACGTTGTGTACATTACGATGCCAATGT 880
ATCACTCTGCCGCCGATCATGGGTATTGGATCATTAAAT 920
TGCATTGGGTGCGACCGCTGTTATTAGGAAAAAGTTTTCG 960
GCAAGCAACTTCTGGAAAGATTGCGTCAAGTACAACGTCA 1000
      1010      1020      1030      1040
      +-----+
CAGCGACACAGTACATTGGAGAAATCTGCAGGTATCTTCT 1040
GGCAGCGAATCCATGTCTGAAGAGAAACAACACAACGTG 1080
CGATTGATGTGGGAAATGGTTTGAGAGGACAAATTTGGA 1120
AAGAGTTTGTAGGAAGATTTGGAATTAAGAAAAATTGGAGA 1160
GTTGTACGGCTCAACAGAAGGAAACTCCAATATTGTTAAC 1200

```

Fig. 78A

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ceFATPb coding only.DNA

1210	1220	1230	1240
GTGGATAACCATGTTGGAGCTTGTGGATT	CATGCCAATTT	1240	
ATCCCCATATTGGATCCCTCTACCCAGTTCGACTTATTAA	1280		
GGTTGATAGAGCCACTGGAGAGCTTGAACGTGATAAGAAC	1320		
GGAATCTGTGTGCCGTGTGTGCCTGGTGAACTGGGGAAA	1360		
TGGTTGGCGTTATCAAGGAGAAAAGATATTCTTCTAAAGTT	1400		
1410	1420	1430	1440
CGAAGGATATGTCAGCGAAGGGGATACTGCAAAGAAAATC	1440		
TACAGAGATGTGTTCAAGCATGGAGATAAGGTGTTTGCAA	1480		
GTGGAGATATTCTTCATTGGGATGATCTTGGATACTTGTA	1520		
CTTTGTGGACCGTTGTGGAGACACTTTCCGTTGGAAAGGG	1560		
GAGAACGTGTCAACTACTGAAGTTGAGGGAATTCTTCAGC	1600		
1610	1620	1630	1640
CTGTGATGGATGTGGAAGATGCAACTGTTTATGGAGTCAC	1640		
TGTCGGTAAAATGGAGGGGCGTGCCGGAATGGCTGGTATT	1680		
GTCGTCAAGGATGGAACGGATGTTGAGAAATTCATCGCCG	1720		
ATATTACTTCTCGACTGACCGAAAAATCTGGCGTCTTACGC	1760		
AATCCCTGTTTTTCATTCCGGCTGTGCAAGGAAGTTGATCGA	1800		
1810	1820	1830	1840
ACCGGAACCTTCAAACCTCAAGAAGACTGATCTTCAAAAAC	1840		
AAGGTTACGACCTGGTTGCTTGTAAGGAGACCCAATTTA	1880		
CTACTGGTCAGCTGCAGAAAAATCCTACAAACCACTGACT	1920		
GACAAAATGCAACAGGATATTGACACTGGTGTTTATGATC	1960		
GCATTTAA	1968		

Fig. 78B



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ceFATPb coding only.protein

10 20 30 40  
MREMPD SPKFALVTFVVYAVVLYNVNSVFWKFVFIGYVVF 40  
RLLRTDFGRRALATLPRDFAGLKLLISVKSTIRGLFKKDR 80  
PIHEIFLNQVKOHPNKVAIIETESGROLTYQELNALANQY 120  
ANLYVSEGYKMGDVVALFMENSIDFFAIWLGLSKIGVYSA 160  
FINSNLKLEPLAHSINVSCKCKSCITNINLLPMFKAAREKN 200  
210 220 230 240  
LISDEIHVFLAGTQVDGRHRSLOQDLHLFSEDEPPVIDGL 240  
NFRSVLCYIYTSGTTGNPKPAVIKHFYFWIAMGAGKAFG 280  
INKSDVVYITMPMYHSAAGIMGIGSLIAFGSTAVIRKKFS 320  
ASNFWKDCVKYNVTATQYIGEICRYLLAANPCPEEKQHN 360  
RLMWGNGLRGDIWKEFVGRFGIKKIGELYGSTEGNSNIVN 400  
410 420 430 440  
VDNHVGACGFMPYIPHIGSLYPVRLIKVD RATGELERDKN 440  
GLCVPCVPGETGEMVGVKEKDILLKFEGYVSEGDTAKKI 480  
YRQVFKHGDQVFASGDILHWDDLGYLYFVDRCGDTFRWKG 520  
ENVSTTEVEGILQPYMVEDATVYGVTVGKMEGRAGMAGI 560  
VVKDGT DVEKFIADITSRLTENLASAIPVFI RLCKEVDR 600  
610 620 630 640  
TGTFKLKKTDLQKQGYDLVACKGDP IYYWSAAEKSYKPLT 640  
DKMQQDIDTGVYDRI. 656

Fig. 79

chFATP coding only.DNA

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10 20 30 40  
ATGGCGTGATGCATCAGGCTCAGCTATACAATGATCTAG 40  
AGGAATTGCTAACTGGTCCATCAGTACCCATCGTTGCTGG 80  
AGCTGCTGGAGCTGCAGCTCTCACTGCCTACATTAACGCC 120  
AAATACCACATAGCCCATGATCTCAAGACCCTCGGTGGTG 160  
GATTGACACAATCGTCCGAAGCGATTGATTTATAAACCG 200  
210 220 230 240  
CCGCGTCGCACAAAAGCGCTCCTCACGCACCACATCTTC 240  
CAGGAGCAGGTCCAAAAACAATCAAATCATCCCTTTCTTA 280  
TCTTTGAGGGCAAGACATGGTCTTACAAGGAGTTCTCTGA 320  
GGCATACACGAGGGTCGCGAACTGGCTGATTGATGAGCTG 360  
GACGTACAAGTAGGGGAGATGGTCGCAATTGATGGCGGAA 400  
410 420 430 440  
ATAGTGCAGAGCACCTGATGCTTTGGCTTGCACTTGATGC 440  
AATCGGTGCGGCTACGAGTTTTTTGAACTGGAACCTGACA 480  
GGGGCAGGGTTAATTCATTGCATAAAGCTATGCGAATGTC 520  
GATTCGTTATCGCAGACATCGATATTAAGCGAACATTGA 560  
ACCGTGCCGTGGCGAACTGGAGGAGACGGGCATCAACATT 600  
610 620 630 640  
CACTACTATGACCCATCCTTCATCTCATCGCTACCGAATA 640  
ACACGCCAATTCCCACAGCCGCACTGAGAACATTGAATT 680  
AGATTCACTACGAGGACTGATATACACATCTGGAACCACT 720  
GGTCTACCTAAAGGCGTGTTTATAAGCACTGGCCGCGAGC 760  
TTAGGACTGACTGGTCGATTTCAAAGTATCTAAATCTCAA 800  
810 820 830 840  
GCCACGGATCGAATGTATACATGTATGCCGCTCTACCAT 840  
GCCGCTGCACACAGCCTCTGTACAGCATCAGTTATTCATG 880  
GTGGAGGTACCGTGGTATTGAGCAGGAAATTCTCACACAA 920  
GAAGTTCTGGCCTGAAGTTGTGGCTTCGGAAGCAAATATC 960  
ATTCAGTACGTTGGTGAATTAGGTCGATATCTCTGAATG 1000  
1010 1020 1030 1040  
GTCCAAAGAGTCCTTACGACAGGGCCCATAAAGTCCAGAT 1040  
GGCGTGGGGCAATGGCATGCGTCCAGACGTGTGGGAAGCG 1080  
TTTCGTGAACGCTTCAACATACCAATTATTCATGAGCTCT 1120  
ATGCCGAACCGATGGGCTCGGGTCAATGACCAATCGTAA 1160  
CGCGGGCCCTTTTACAGCAAACGTATTGCGCTGCGAGGG 1200

Fig. 80A

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chFATP coding only.DNA

---

1210      1220      1230      1240

---

CTGATCTGGCACTGGAAATTTTCGAAATCAGGAAGTGCTGG 1240  
TCAAGATGGATCTCGATACTGATGAGATCATGAGAGATCG 1280  
CAATGGGTTTGGCATAACGATGCGCTGTCAATGAACCTGGA 1320  
CAGATGCTTTTTTCGGCTGACACCCGAAACTCTGGCTGGTG 1360  
CACCAAGCTACTACAACAACGAAACGGCCACACAGAGCAG 1400

---

1410      1420      1430      1440

---

GCGGATTACAGATGTGTTTTCAAAGGGTGACCTGTGGTTC 1440  
AAGTCCGGTGACATGCTACGGCAAGACGCCGAAGGCCGCG 1480  
TCTACTTTGTGATCGACTAGGCGATACGTTCCGCTGGAA 1520  
ATCCGAAAACGTTTCTACCAATGAAGTCGCGGACGTGATG 1560  
GGCACATTTCTCAGATTGCTGAAACGAATGTATACGGTG 1600

---

1610      1620      1630      1640

---

TCCTTGTGCCGGGTAAACGATGGTTCGAGTGCGCAGCCTCAA 1640  
TTGTCATGGCAGACGGCGTGACAGAGTCGACATTCGCTTC 1680  
GCTGCCCTTGCAAAGCACGCCCGAGATCGGTTACCGGGTT 1720  
ATGCTGTACCACTGTTTCTGAGGGTAACTCCAGCACTTGA 1760  
ATATACGGGCACATTAAGATTTCAGAAAGGACGCCTCAAG 1800

---

1810      1820      1830      1840

---

CAGGAAGGTATAGACCCAGATAAGATTTCCGGCGAAGATA 1840  
AGTTATACTGGCTGCCGCCTGGTAGCGATATATATTTACC 1880  
ATTTGGAAAGATGGAGTGGCAGGGAATTGTAGATAAGCGT 1920  
ATACGGCTGTGA 1932

Fig. 80B

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chFATP coding only, protein

```
      10      20      30      40
MACMHQAQLYNDLEELLTGPSVPIVAGAAGAAALTAYINA 40
KYHIAHDLKTLGGGLTOSSEAI DF INRRVAQKRVLTHHIF 80
QEQVKQKSNHPFLIFEGKTWSYKEFSEAYTRVANWLIDEL 120
DVQVGEMVAIDGGNSAEHMLWLALDAIGAATSFLNWNLT 160
GAGLIHCIKLCECRFVIADIDIKANIEPCRGELEETGINI 200
      210      220      230      240
HYYDPSFISSLPNNTPIPD SR TENIELDSVRGLIYTS GTT 240
GLPKGVFI STGRELRTOWSISKYLN LKPTDRMYTCMP LYH 280
AAAHSLCTASVIHGGGT VVLSRKFSHKKFWPEVVASEANI 320
IQYVGELGRYLLNGPKSPYDRAHKVQMAWGNGMRPDVWEA 360
FRERFNIPIIHEL YAATDGLGSMTNRNAGPFTANCIALRG 400
      410      420      430      440
LIWHWKFRNQEVLVKMDLDTDEIMRDRNGFAIRCAVNEPG 440
QMLFRLTPETLAGAPSYNNETATQSRRI TOVFQKGDLWF 480
KSGDMLRQDAEGRVYFVDRLGDTFRWKSENVSTNEVADVM 520
GTFPQIAETNVYGVLPVGN DGRVRS LNCHGRRRORVDIRF 560
AALAKHARDRLPGYAVPLFLRVTPALEYTGTLKIQKGR LK 600
      610      620      630      640
QEGIDPDKISGEDKLYWLP PGSDIYLPFGKMEWQGI VDKR 640
IRL 643
```

Fig. 81

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aspergillus partial.DNA

```
      10      20      30      40
      |      |      |      |
CTTTACCATTCATCAGCTTCATTCTGCATTTTGTAGCTTGA 40
CGGCAGCCGGGTCTACGCTGATCATCGGCCGCAAGTTCTC 80
CGCGAGAACTTCATAAAGGAAGGCGCGGAGAACGACGCC 120
ACGGTCATCCAGTACGTGGGTGAGACCTTGCGATATCTGC 160
TCGCCACCCCGGTGAAACCGATCCAGTTACTGGCGAAGA 200
      210      220      230      240
      |      |      |      |
CCTGGACAAAAAGCACAAATATTCGAGCAGTATACGGCAAC 240
GGGCTACGGCCGGATATCTGGAACCGCTTCAAGGAGCGCT 280
TCAACGTGCCGACGGTTGCCGAATTTTATGCTGCAACCGA 320
GAGCCCAGGCGGAACATGGAACATTCAACAAATGACTTC 360
ACTGCCGGAGCCATTGGGCACACTGGCGTGCTTAGTGGAT 400
      410      420      430      440
      |      |      |      |
GGCTTCTTGACGCGGCCTTACTATTGTGCGAGGTGGACCA 440
GGAATCACAGGAACCATGGCGCGATCCCCAAACCGGGTTC 480
TGCAAGCCGGTCCCGCGAGGCGAAGCAGGCGAGCTCCTGT 520
ATGCCATTGATCCGGCCGACCCGGGCGAGACCTTCAGGG 560
CTACTACCGCAACTCCTTTAGAGCACACTGGCGGCCG 597
```

Fig. 82

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aspergillus partial.protein

10 20 30 40  
LYHSSASFCIFSLTAAGSTLIIGRKFSARNFIKEAREND 40  
TVIQYVGETLRYLLATPGETOPVTGEDLDKKHNIRAVYGN 80  
GLRPDIWNRKERNVPTVAEFYAATESPGGTWNYSTNDF 120  
TAGAIGHTGVLSGWLLGRGLTIVEVDQESQEPWRDPQTGF 160  
CKPVPRGEAGELLYAIDPADPGETFQGYRNSFRAHWRP 199

Fig. 83

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mgFATP partial.DNA

```
      10      20      30      40
      |      |      |      |
GCAAAGGCCGACGCGTGGCTGCGGACGGGTAACGTGATCA 40
GGGCGGACAACGAAGGGCGACTCTTCTTCCACGACCGGAT 80
CGGAGACACGTTCCGATGGAAGGGAGAGACNGTCAGCACA 120
CAAGAGGTCAGTTTGGTGCTCGGACGACACGACTCAATCA 160
AGGAGGCCAACGTGTACGGCGTGACGGTGCCGAACCACGA 200
      210      220      230      240
      |      |      |      |
CGGGCGGGCCGGCTGCGCTGCGCTCACGCTATCAGACGCT 240
CTGGCGACTGAAAAGAAGCTGGGCGATGAGCTGCTAAAGG 280
GATTGGCTACTCACTCGTCGACTTCGCTTCCCAAGTTTGC 320
GGTGCCGAGTTTCTACGGGTGGTGCGCGGCGAGATGCAG 360
TCAACGGGCACCAACAAGCAACAGAAGCACGACCTGAGGG 400
      410      420      430      440
      |      |      |      |
TGCAGGGTGTAGAGCCGGGCAAGGTGGGCGTAGACGAGGT 440
GTACTGGTTGCGGGGAGGGACATATGTACCATTCGGAACA 480
GAGGATTGGGATGGGTGAAGAAGGGCTTGTGAAGTTGT 520
GA 522
```

Fig. 84

mgFATP partial.protein

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10 20 30 40

---

AKADAWLRTGNVIRADNEGRLFFHDRIGDTFRWKGETVST 40  
QEVSLVLGRHDSIKEANYYGVTVPNHOGGRAGCAALTLSOA 80  
LATEKKLGDELLKGLATHSSTSLPKFAVPQFLRVVRGEMQ 120  
STGTNKQOKHDLRVQGVPEPGKVGVDVYWL RGGTYVPFGT 160  
EDWDGLKKGLVKL 173

Fig. 85



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scFATP coding only.DNA

10 20 30 40  
ATGTCTCCCATACAGGTTGTTGTCTTTGCCTTGTCAAGGA 40  
TTTTCTGCTATTATTCAGACTTATCAAGCTAATTATAAC 80  
CCCTATCCAGAAATCACTGGGTTATCTATTTGGTAATTAT 120  
TTTGATGAATTAGACCGTAAATATAGATACAAGGAGGATT 160  
GGTATATTATTCCTTACTTTTTGAAAAGCGTGTTTTGTTA 200  
210 220 230 240  
TATCATTGATGTGAGAAGACATAGGTTTCAAACTGGTAC 240  
TTATTTATTAAACAGGTCCAACAAAATGGTGACCATTTAG 280  
CGATTAGTTACACCCGTCCCATGGCCGAAAAGGGAGAATT 320  
TCAACTCGAAACCTTTACGTATATTGAAACTTATAACATA 360  
GTGTTGAGATTGTCTCATATTTTGCATTTTGATTATAACG 400  
410 420 430 440  
TTCAGGCCGGTGACTACGTGGCAATCGATTGTACTAATAA 440  
ACCTCTTTTCGTATTTTTATGGCTTTCTTTGTGGAACATT 480  
GGGGCTATTCCAGCTTTTTTAACTATAATACTAAAGGCA 520  
CTCCGCTGGTTCACTCCCTAAAGATTTCCAATATTACGCA 560  
GGTATTTATTGACCCTGATGCCAGTAATCCGATCAGAGAA 600  
610 620 630 640  
TCGGAAGAAGAAATCAAAAACGCCTTCTGATGTTAAAT 640  
TAACTATCTTGAAGAACAAGACTTAATGCATGAACTTTT 680  
AAATTCGCAATCACCGGAATTCTTACAACAAGACAACGTT 720  
AGGACACCACTAGGCTTGACCGATTTTAAACCCTCTATGT 760  
TAATTTATACATCTGGAACCACTGGTTTGCCTAAATCCGC 800  
810 820 830 840  
TATTATGTCTTGGAGAAAATCCTCCGTAGGTTGTCAAGTT 840  
TTTGGTCATGTTTTACATATGACTAATGAAAGCACTGTGT 880  
TCACAGCCATGCCATTGTTCCATTCAACTGCTGCCTTATT 920  
AGGTGCGTGCGCCATTCTATCTCACGGTGGTTGCCTTGCG 960  
TTATCGCATAAAATTTCTGCCAGTACATTTTGAAGCAAG 1000  
1010 1020 1030 1040  
TTTATTTAACAGGAGCCACGCACATCCAATATGTCGGAGA 1040  
AGTCTGTAGATACCTGTTACATACGCCAATTTCTAAGTAT 1080  
GAAAAGATGCATAAGGTGAAGGTTGCTTATGGTAACGGGC 1120  
TGAGACCTGACATCTGGCAGGACTTCAGGAAGAGGTTCAA 1160  
CATAGAAGTTATTGGTGAATTCTATGCCGCAACTGAAGCT 1200

Fig. 86A

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scFATP coding only.DNA

1210	1220	1230	1240
CCTTTTGCTACAACCTACCTTCCAGAAAGGTGACTTTGGAA 1240			
TTGGCGCATGTAGGAACTATGGTACTATAATTCAATGGTT 1280			
TTTGTCAATCCAACAAACATTGGTAAGGATGGACCCAAAT 1320			
GACGATTCCGTTATATATAGAAATTCCAAGGGTTTCTGCG 1360			
AAGTGGCCCCCTGTTGGCGAACCAGGAGAAATGTTAATGAG 1400			
1410	1420	1430	1440
AATCTTTTTCCCTAAAAAACCAGAAACATCTTTTCAAGGT 1440			
TATCTTGGTAATGCCAAGGAAACAAAGTCCAAAGTTGTGA 1480			
GGGATGTCTTCAGACGTGGCGATGCTTGGTATAGATGTGG 1520			
AGATTTATTTAAAAGCGGACGAATATGGATTATGGTATTTT 1560			
CTTGATAGAATGGGTGATACTTTTCAGATGGAAATCTGAAA 1600			
1610	1620	1630	1640
ATGTTTCCACTACTGAAGTAGAAGATCAGTTGACGGCCAG 1640			
TAACAAAGAACAATATGCACAAGTTCTAGTTGTTGGTATT 1680			
AAAGTACCTAAATATGAAGGTAGAGCTGGTTTTGCAGTTA 1720			
TTAAACTAACTGACAACCTCTCTTGACATCACTGCAAAGAC 1760			
CAAATTATTAAATGATTCCTTGAGCCGGTTAAATCTACCG 1800			
1810	1820	1830	1840
TCTTATGCTATGCCCCTATTTGTTAAATTTGTTGATGAAA 1840			
TTAAATGACAGATAACCTCATAAAATTTTGA 1872			

Fig. 86B

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scFATP coding only.protein

```
      10      20      30      40
MSPIQVVVFALSRI FLLLFRLIKLIITPIQKSLGYLFGNY 40
FOELDRKYRYKEOWYIIPYFLKSVFCYIIDVRRHRFONWY 80
LFIKQVQONGDHLAISYTRPMAEKGEFQLETFTYIETYN I 120
VLRLSHILHFDYNVOAGDYVAIDCTNKPLFVFLWLSLWNI 160
GAIPAFLNYNTKGTPLVHSLKISNITQVFI DPDASNPIRE 200
      210      220      230      240
SEEEIKNALPDVKLNYLEEQDLMHELLNSQSPEFLQDDNV 240
RTPLGLTDFKPSMLIYTSGTTGLPKSAIMSWRKSSVGCQV 280
FGHVLHMTNESTVFTAMPLFHSTAALLGACAILSHGGCLA 320
LSHKFSASTFWKQVYLTGATHIQYVGEVCRYLLHTPISKY 360
EKMHKVKVAYGNGLRPDIWQDFRKRFNIEVIGEFYAATEA 400
      410      420      430      440
PFATTTTQKGDFGIGACRNYGTIIQWFLSFQQTIVRMDPN 440
DDSVIYRNSKGFCEVAPVGEPGEMLMRIFFPKKPETSFOG 480
YLGNAKETKSKVVRDVFRRGDAWYRCGDLLKADEYGLWYF 520
LORMGDTFRWKSENVSTTEVEDQLTASNKEQYAQVLVVG I 560
KVPKYEGRAGFAVIKLTDSLDTAKTKLLNDSLRLNLP 600
      610      620      630      640
SYAMPLFVKFVDEIKMTDNLIK F. 624
```

Fig. 87

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mtFATP coding only.DNA

```

      10      20      30      40
+-----+
GTGTCCGATTACTACGGCGGGCGCACACACAACGGTCAGGC 40
TGATCGACCTGGCAACTCGGATGCCGCGAGTGTTGGCGGA 80
CACGCCGGTGATTGTGCGTGGGGCAATGACCGGGCTGCTG 120
GCCCCGGCGAATTCCAAGGCGTCGATCGGCACGGTGTTCC 160
AGGACCGGGCGCTCGCTACGGTGACCGAGTCTTCTGAA 200
      210      220      230      240
+-----+
ATTGCGCGATCAGCAGCTGACCTACCGCGACGCTAAGGCC 240
ACCGCCAACCGGTACGCCGCGGTGTTGGCCGCCCGCGCG 280
TCGCCCCCGGCGACGTCGTTGGCATCATGTTGCGTAACTC 320
ACCCAGCACAGTCTTGCGGATGCTGGCCACGGTCAAGTGC 360
GGCGCTATCGCCGGCATGCTCAACTACCACGAGCGCGGCG 400
      410      420      430      440
+-----+
AGGTGTTGGCGCACAGCCTGGGTCTGCTGGACGCGAAGGT 440
ACTGATCGCAGAGTCCGACTTGGTCAGCGCCGTCGCCGAA 480
TGCGGGCGCTTCGCGCGGCCGGGTAGCGGGCGACGTGCTGA 520
CCGTCGAGGACGTGGAGCGATTTCGCCACAACGGCGCCCGC 560
CACCAACCCGGCGTCGGCGTCGGCGGTGCAAGCCAAAGAC 600
      610      620      630      640
+-----+
ACCGCGTTCTACATCTTCACCTCGGGCACCAACCGGATTTT 640
CCAAGGCCAGTGTCATGACGCATCATCGGTGGCTGCGGGC 680
GCTGGCCGCTTTCGGAGGGATGGGGCTGCGGCTGAAGGGT 720
TCCGACACGCTCTACAGCTGCCTGCCGCTGTACCACAACA 760
ACGCGTTAACGGTCGCGGTGTCGTGCGGTGATCAATTCTGG 800
      810      820      830      840
+-----+
GGCGACCCTGGCGCTGGGTAAGTCGTTTTTCGGCGTCGCGG 840
TTCTGGGATGAGGTGATTGCCAACCGGGCGACGGCGTTTCG 880
TCTACATCGGCGAAATCTGCCGTTATCTGCTCAACCAGCC 920
GGCCAAGCCGACCGACCGTGCCCAACAGGTGCGGGTGATC 960
TGCGGTAACGGGCTGCGGCCGGAGATCTGGGATGAGTTCA 1000
      1010      1020      1030      1040
+-----+
CCACCCGCTTCGGGGTCGCGCGGGTGTCGAGTTCTACGC 1040
CGCCAGCGAAGGCAACTCGGCCTTTATCAACATCTTCAAC 1080
GTGCCCAGGACCGCGGGGTATCGCCGATGCCGCTTGCTT 1120
TTGTGGAATACGACCTGGACACCGGCGATCCGCTGCGGGA 1160
TGCGAGCGGGCGAGTGCGTCGGGTACCCGACGGTGAACCC 1200

```

Fig. 88A

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mtFATP coding only.DNA

1210	1220	1230	1240
GGCCTGTTGCTTAGCCGGGTCAACCGGCTGCAGCCGTTCC	1240		
ACGGCTACACCGACCCGGTTGCCAGCGAAAAGAAGTTGGT	1280		
GCGCAACGCTTTTCGAGATGGCGACTGTTGGTTCAACACC	1320		
GGTGACGTGATGAGCCCGCAGGGCATGGGCCATGCCGCCT	1360		
TCGTCGATCGGCTGGGCGACACCTTCCGCTGGAAGGGCGA	1400		
1410	1420	1430	1440
GAATGTCGCCACCACTCAGGTCGAAGCGGCACTGGCCTCC	1440		
GACCAGACCGTCGAGGAGTGCACGGTCTACGGCGTCCAGA	1480		
TTCCGCGCACCGGCGGGCGCGCCGGAATGGCCGCGATCAC	1520		
ACTGCGCGCTGGCGCCGAATTTCGACGGCCAGGCGCTGGCC	1560		
CGAACGGTTTACGGTCACTTGCCCGGCTATGCACTTCCGC	1600		
1610	1620	1630	1640
TCTTTGTTCCGGTAGTGGGGTCGCTGGCGCACACCACGAC	1640		
GTTCAAGAGTCGCAAGGTGGAGTTGCGCAACCAGGCCTAT	1680		
GGCGCCGACATCGAGGATCCGCTGTACGTACTGGCCGGCC	1720		
CGGACGAAGGATATGTGCCGTACTACGCCGAATACCCTGA	1760		
GGAGGTTTCGCTCGGAAGGCGACCGCAGGGCTAG	1794		

Fig. 88B

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mtFATP coding only.protein

```
      10      20      30      40
MSOYYGGAHTTVRLIDLATRMPRVLADTPVIVRGAMTGLL 40
ARPNKASIGTVFQDRAARYGDRVFLKFGDQQLTYRDANA 80
TANRYAAVLAARGVGPGDVVGIMLRNSPSTVLAMLATVKC 120
GAIAGMLNYHQGEVLAHSLGLLDQAKVLAESDLVSAVAE 160
CGASRGRVAGOVLTVEDVERFATTAPATNPASASAVQAKD 200
      210      220      230      240
TAFYIFTSGTTGFPKASVMTHHRWLRALAVFGGMGLRLKG 240
SDTLYSCLPLYHNNALTVAVSSVINSGLATLALGKSFSASR 280
FWDEVIANRATAFVYIGEICRYLLNOPAKPTDRAHQVRVI 320
CGNGLRPEIWDEFTTRFGVARVCEFYAASEGNSAFINIFN 360
VPRTAGVSPMPLAFVEYDLDTGQPLRDASGRVRRVPDGEF 400
      410      420      430      440
GLLLSRVNRLOPFDGYTDPVASEKKLVRNAFRDGCWFNT 440
GDVMSPOGMGHAAFVDRLGDFRWKGENVATTQVEAALAS 480
DQTVEECTVYGVQIPRTGGRAGMAAITLRAGAEFDGQALA 520
RTVYGHLPGYALPLFVRVVGSLAHTTTFKSRKVELRNOAY 560
GADIEDPLYVLGPDEGYVPYYAEYPEEVSLGRRPOG. 598
```

Fig. 89

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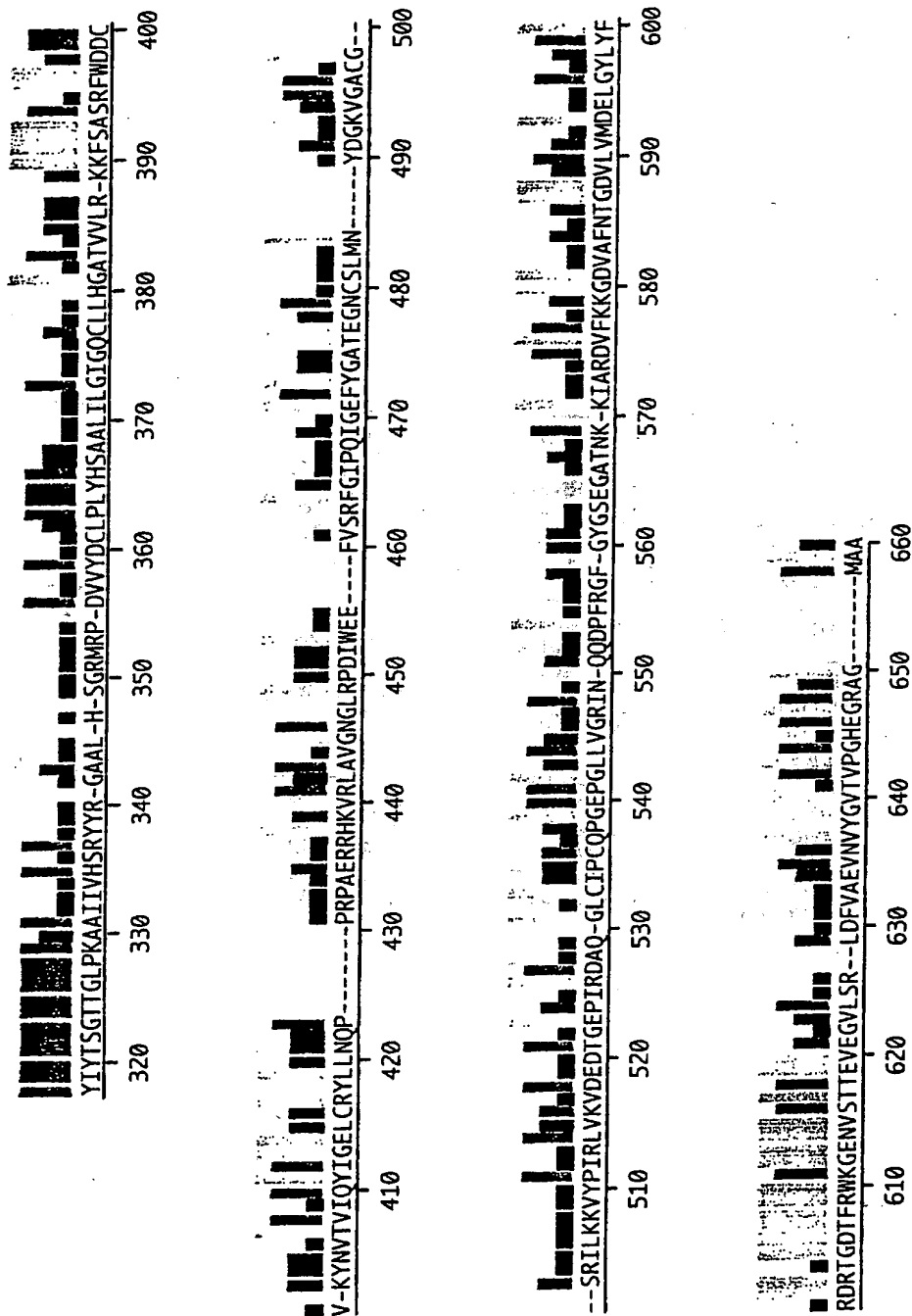


Figure 90

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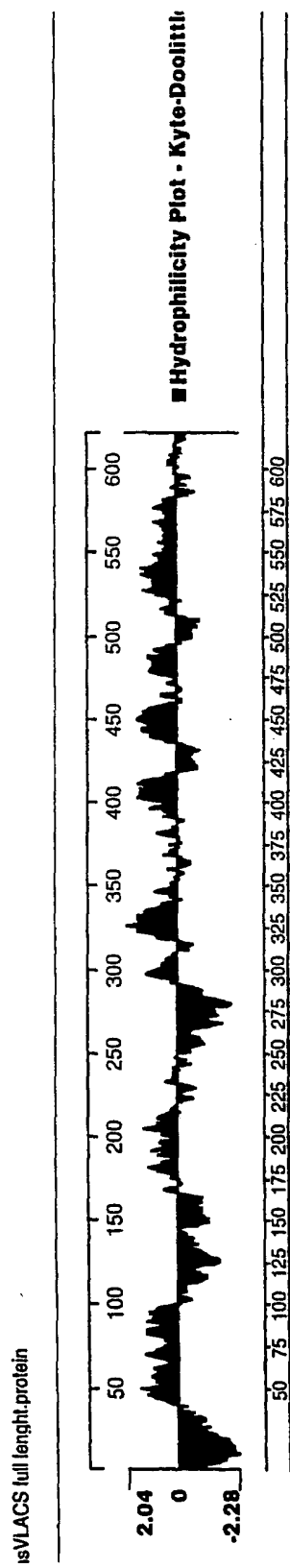
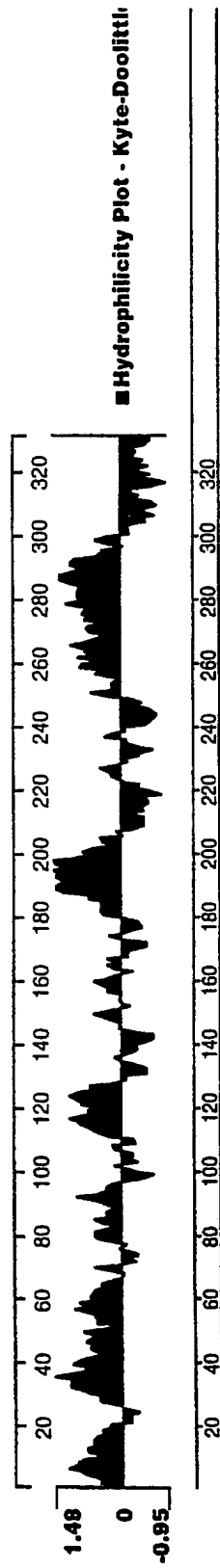


Figure 91

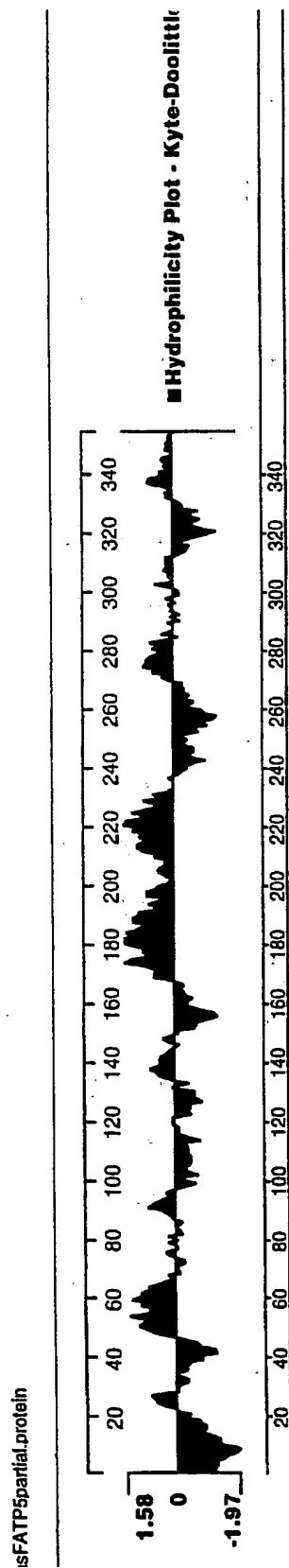


rsFATP3partial.protein



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Figure 92



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Figure 93

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## hsFATP3

```
1      cga ccc acg cgt ccg ggg atg ttt gcg agc ggc tgg aac cag acg gtg ccg ata gag gaa
1      M F A S G W N Q T V P I E E

61     gcg ggc tcc atg gct gcc ctc ctg ctg ctg ccc ctg ctg ctg ttg cta ccg ctg ctg ctg
15     A G S M A A L L L L P L L L L L P L L L

121    ctg ctg aag cta cac ctc tgg ccg cag ttg cgc tgg ctt ccg gcg gac ttg gcc ttt gcg
35     L L K L H L W P Q L R W L P A D L A F A

181    gtg cga gct ctg tgc tgc aaa agg gct ctt cga gct cgc gcc ctg gcc gcg gct gcc gcc
55     V R A L C C K R A L R A R A L A A A A A

241    gac ccg gaa ggt ccc gag ggg ggc tgc agc ctg gcc tgg cgc ctc gcg gaa ctg gcc cag
75     D P E G P E G G C S L A W R L A E L A Q

301    cag cgc gcc gcg cac acc ttt ctc att cac ggc tcg cgg cgc ttt agc tac tca gag gcg
95     Q R A A H T F L I H G S R R F S Y S E A

361    gag cgc gag agt aac agg gct gca cgc gcc ttc cta cgt gcg cta ggc tgg gac tgg gga
115    E R E S N R A A R A F L R A L G W D W G

421    ccc gac ggc ggc gac agc ggc gag ggg agc gct gga gaa ggc gag cgg gca gcg ccg gga
135    P D G G D S G E G S A G E G E R A A P G

481    gcc gga gat gca gcg gcc gga agc ggc gcg gag ttt gcc gga ggg gac ggt gcc gcc aga
155    A G D A A A G S G A E F A G G D G A A R

541    ggt gga gga gag ccc gcc gcc cct ctg tca cct gga gca act gtg gcg ctg ctc ctc ccc
175    G G G E P A A P L S P G A T V A L L L P

601    gct ggc cca gag ttt ctg tgg ctc tgg ttc ggg ctg gcc aag gcc ggc ctg cgc act gcc
195    A G P E F L W L W F G L A K A G L R T A

661    ttt gtg ccc acc gcc ctg cgc cgg ggc ccc ctg ctg cac tgc ctc cgc agc tgc ggc gcg
215    F V P T A L R R G P L L H C L R S C G A

721    cgc gcg ctg gtg ctg gcg cca gag ttt ctg gag tcc ctg gag ccg gac ctg ccc gcc ctg
235    R A L V L A P E F L E S L E P D L P A L

781    aga gcc atg ggg ctc cac ctg tgg gct gca ggc cca gga acc cac cct gct gga att agc
255    R A M G L H L W A A G P G T H P A G I S

841    gat ttg ctg gct gaa gtg tcc gct gaa gtg gat ggg cca gtg cca gga tac ctc tct tcc
275    D L L A E V S A E V D G P V P G Y L S S

901    ccc cag agc ata aca gac acg tgc ctg tac atc ttc acc tct ggc acc acg ggc ctc ccc
395    P Q S I T D T C L Y I F T S G T T G L P

961    aag gct gct cgg atc agt cat ctg aag atc ctg caa tgc cag ggc ttc tat cag ctg tgt
315    K A A R I S H L K I L Q C Q G F Y Q L C

1021   ggt gtc cac cag gaa gat gtg atc tac ctc gcc ctc cca ctc tac cac atg tcc ggt tcc
335    G V H Q E D V I Y L A L P L Y H M S G S

1081   ctg ctg ggc atc gtg ggc tgc atg ggc att ggg gcc aca gtg gtg ctg aaa tcc aag ttc
355    L L G I V G C M G I G A T V V L K S K F

1141   tcg gct ggt cag ttc tgg gaa gat tgc cag cag cac agg gtg acg gtg ttc cag tac att
375    S A G Q F W E D C Q Q H R V T V F Q Y I

1201   ggg gag ctg tgc cga tac ctt gtc aac cag ccc ccg agc aag gca gaa cgt ggc cat aag
395    G E L C R Y L V N Q P P S K A E R G H K
```

Figure 94A

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1261 gtc cgg ctg gca gtg ggc agc ggg ctg cgc cca gat acc tgg gag cgt ttt gtg cgg cgc  
415 V R L A V G S G L R P D T W E R F V R R

1321 ttc ggg ccc ctg cag gtg ctg gag aca tat gga ctg aca gag ggc aac gtg gcc acc atc  
435 F G P L Q V L E T Y G L T E G N V A T I

1381 aac tac aca gga cag cgg ggc gct gtg ggg cgt gct tcc tgg ctt tac aag cat atc ttc  
455 N Y T G Q R G A V G R A S W L Y K H I F

1441 ccc ttc tcc ttg att cgc tat gat gtc acc aca gga gag cca att cgg gac ccc cag ggg  
475 P F S L I R Y D V T T G E P I R D P Q G

1501 cac tgt atg gcc aca tct cca ggt gag cca ggg ctg ctg gtg gcc cgg gta agc cag cag  
495 H C M A T S P G E P G L L V A P V S Q Q

1561 ccc cca ttc ctg ggc tat gct ggc ggg cca gag ctg gcc cag ggg aag ttg cca aag gat  
515 S P F L G Y A G P E L A Q G K L L K D

1621 gtc ttc cgg cct ggg gat gtt ttc ttc aac act ggg gac ctg ctg gtc tgc gat gac caa  
535 V F R P G D V F F N T G D L L V C D D Q

1681 ggt ttt ctg cgc ttc cat gat cgt act gga gac acc ttc agg tgg aag ggg gag aat gtg  
555 G F L R F H D R T G D T F R W K G E N V

1741 gcc aca acc gag gtg gca gag gtc ttc gag gcc cta gat ttt ctt cag gag gtg aac gtc  
575 A T T E V A E V F E A L D F L Q E V N V

1801 tat gga gcc act gtg cca ggg cat gaa ggc agg gct gga atg gca gcc cta gtt ctg cgt  
595 Y G V T V P G H E G R A G M A A L V L R

1861 ccc ccc cac gct ttg gac ctt atg cag ctg tac acc cac gtg tct gag aac ttg cca cct  
615 P P H A L D L M Q L Y T H V S E N L P P

1921 tat gcc cgg ccc cga ttc ctg agg ctg cag gag tct ttg gcc acc aca gag acc ttc aaa  
635 Y A R P R F L R L Q E S L A T T E T F K

1981 cag cag aaa gtt cgg atg gca aat gag ggc ttc gac ccc agc acc ctg tct gac cca ctg  
655 Q Q K V R M A N E G F D P S T L S D P L

2041 tac gtt ctg gac cag gct gta ggt gcc tac ctg ccc ctg aca act gcc cgg tac agc gcc  
675 Y V L D Q A V G A Y L P L T T A R Y S A

2101 ctg ctg gca gga aac ctt cga atc tga gaa ctt cca cac ctg agg cac ctg aga gag gaa  
695 L L A G N L R I \*

2161 ctg tgt

Figure 94B